OFFICE OF NAVAL RESEARCH
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TASK NO. NR 202-043

FINAL REPORT

TWO-YEAR FEEDING STUDY IN RATS

BY

E. ROSS HART, PH.D.

LITTON BIONETICS, INC.
5516 NICHOLSON LANE
KENSINGTON, MARYLAND 20795

27 August 1976

This research was performed for the Office of Naval Research, Biochemistry Program, Navy Biology Project, under contract No. N00014-73-C-0162, NR 202-043 and sponsored by the Naval Medical Research and Development Command.

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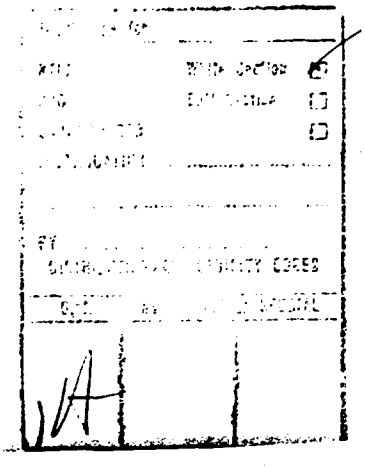

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Incorporation of RDX in the diets of rats at levels of 1.0, 3.1, and 10 mg/kg over a two-year period did not lead to appearance of important evidence of toxicity.

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SPONSOR: Office of Naval Research DATE: August 27, 1976

MATERIAL: RDX

SUBJECT: FINAL REPORT
Two-Year Feeding Study in Rats
LBI Project No. 1400

SUMMARY

Incorporation of RDX in the diets of rats at levels of 1.0, 3.1, and 10 mg/kg over a two-year period did not lead to appearance of important evidence of toxicity.

SPONSOR: Office of Naval Research DATE: August 27, 1976

MATERIAL: RDX

SUBJECT: FINAL REPORT
Two-Year Feeding Study in Rats
LBI Project No. 1400

1. OBJECTIVE

The objective of this chronic feeding study was to evaluate the toxicity and pharmacologic effect of RDX when administered to male and female rats over their lifetime in an attempt to simulate the exposure that may be experienced by man when substances may be ingested for prolonged periods.

2. MATERIAL

The test material, labelled RDX, was received from the Office of Naval Research in September 1973, and was assigned BRL No. 726A. The material as received was a course white granular mixture moistened with alcohol. Additional quantities of the test material were received on January 15, 1974, May 16, 1974, October 2, 1974, and June 2, 1975, and were assigned BRL numbers 726B, 726C, 726D, and 726E, respectively.

3. EXPERIMENTAL DESIGN

A. Animals

The study was carried out in rats of the Charles River Sprague-Dawley strain with body weights averaging 98.5 grams for males and 87.9 grams for females at initiation.

B. Animal Groups

The rats were randomly assigned to the following groups:

Group No.	No. of Animals		Daily Dosage
	Male	Female	mg/kg
1	100	100	Zero - Control
2	100	100	Low - 1.0
3	100	100	Intermediate - 3.1
4	100	100	High - 10

3. EXPERIMENTAL DESIGN (Continued)

C. Diet Preparation

To minimize the explosive hazard of the dry RDX alone, a supply of the fine granular material was provided. It was supplied in preweighed, 5 gm portions packaged in plastic snap-top containers and wetted with 30% ethanol in water. A premix of RDX in ground rat chow was prepared in sufficient concentration and quantity to completely use one 5 gm portion. This premix was then used to prepare, on a weight/weight basis, the appropriate diet for each group.

D. Housing

Twenty-five (25) rats of each sex of each control or treatment group were housed individually in wire bottom cages. The others were housed in groups of three by sex in solid bottom plastic cages with sawdust bedding.

E. Observations

For those rats housed individually, body weights and food consumption were recorded weekly for the first 26 weeks, biweekly for the next 26 weeks, and every 4 weeks thereafter. Daily mortality checks were made on all rats regardless of housing, as were weekly records of appearance, behavior, and signs of toxic or pharmacologic effects.

F. Clinical Laboratory Measurements

The following clinical studies were performed on 10 male and 10 female animals from the control and each test group:

Hematology at 13, 26, 52, and 104 weeks, including:

hematocrit	total leukocyte count
hemoglobin	differential leukocyte count
erythrocyte count	reticulocyte count

Blood Chemistry at 52 and 104 weeks, including:

fasting blood sugar	serum potassium	serum alkaline phosphatase
blood urea nitrogen	serum chloride	serum glutamic-oxaloacetic transaminase
total serum protein	serum glutamic-pyruvic transaminase	
total serum bilirubin	methemoglobin	
serum sodium		

3. EXPERIMENTAL DESIGN (Continued)

F. Clinical Laboratory Measurements

Urinalysis, using pooled samples per group at 13, 26, 52 and 104 weeks, including:

pH	bilirubin
specific gravity	microscopic examination of sediment
glucose	urine glutamic-oxaloacetic transaminase
ketones	

G. Interval Necropsies

At 52 weeks, 10 male and 10 female animals from the control and each test group were killed and gross necropsies performed. These animals were selected at random from the groups which were group housed. Those organs to be taken at termination (see below) were preserved in buffered 10% formalin. Organ weights were recorded for liver, kidneys, thyroids and adrenals.

H. Termination

The study was terminated at 104 weeks and all surviving rats were necropsied.

I. Organ Weights

The weights of the following organs were recorded for each rat:

thyroids (after fixation)	kidneys
heart	adrenals (after fixation)
liver	testes with epididymis
spleen	

J. Tissue Preservation

The following tissues from each rat were preserved in buffered 10% formalin:

brain	spleen	testes with epididymis
pituitary	kidneys	seminal vesicles
thoracic spinal cord	adrenals	ovary
	stomach	uterus
eye	pancreas	skin
thyroids	small intestine	rib junction
lung	large intestine	bone marrow
heart	mesenteric lymph node	nerve with muscle
liver		any unusual lesions
	urinary bladder	

3. EXPERIMENTAL DESIGN (Continued)

K. Histopathologic Examination

The following tissues from all animals from the control and the high level test group were examined microscopically after the interval and terminal sacrifices:

pituitary	adrenals	urinary bladder
thyroids	stomach	testes
heart	pancreas	ovary
liver	small intestine	bone marrow
spleen	large intestine	any unusual lesions
kidneys	mesenteric lymph node	

The target organs from the animals in the intermediate and the low level test groups were examined microscopically. Pathological examination was made of the organs of those animals that died during the course of the study in the control and the high level groups when autolysis did not make this impractical.

L. Statistical Analysis

The tabular presentations of numerical data in the Results Section include means and standard errors by group and sex. It is our standard policy to express means with the same degree of precision (i.e., number of decimal places) as the original data and to express standard error to two significant digits regardless of decimal places.

4. RESULTS

During the night preceding Day 76 of this study, there was a malfunction of the heating system in the building that resulted in excessive rises in temperature in animal rooms. A total of 59 rats assigned to this study were found dead. It seemed appropriate to deduct these from the "starting" population and report survival accordingly. On this basis survival was:

4. RESULTS (Continued)

	Males				Females			
	Control	Low	Med.	High	Control	Low	Med.	High
Initial Pop.	100	100	100	100	100	100	100	100
Deaths Due To Overheating	6	5	14	8	17	5	0	4
Deaths 1st. Yr.	1	3	3	4	0	1	5	2
Interim Kill	10	10	10	10	10	10	10	10
SURVIVORS								
12 Mo.	83	82	73	78	73	84	85	84
18 Mo.	77	77	70	75	70	80	83	78
19 Mo.	73	75	69	74	70	78	82	75
20 Mo.	68	72	66	70	68	75	81	69
21 Mo.	64	68	63	66	64	72	78	65
22 Mo.	60	66	63	63	62	67	70	62
23 Mo.	55	59	57	57	59	59	68	59
24 Mo.	50=60%	55=67%	51=70%	49=63%	53=73%	53=63%	61=72%	53=63%

It seems clear that the differences between groups are not important.

Body weights are presented as group means in Table 1. The few instances of statistically significant differences do not indicate important toxicity.

Food consumption measurements are similarly presented in Table 2. Again no important effects are seen.

Hematocytology results, as presented in Table 3, show a questionable tendency toward fluctuations in red cell counts, reticulocyte counts, cell volumes and hemoglobin values but no clear dose-effect trends occurred to result in a conclusion of compound effect.

The blood chemistry values presented in Table 4 show a few statistically significant differences particularly in electrolytes. However, these barely meet the criterion for significance and do not seem toxicologically important. Urinalysis results, presented in Table 5, all seem normal. Postmortem organ weights, presented as measured in Table 6 and as calculated percentage of terminal body weight in Table 7, indicate no important toxicity.

The gross necropsy findings are listed in Table 8. Again no important toxicity is noted.

A summary of the histopathology findings signed by the pathologist who examined the slides is attached together with a tabulation of the incidence of findings. Once again, no important toxicity is noted.

5. CONCLUSIONS

Incorporation of RDX in the diets of rats at levels of 1.0, 3.1 and 10 mg/kg over a two-year period did not lead to appearance of important evidence of toxicity.

Submitted by:

E. Ross Hart, Ph.D.
Director
Department of Pharmacology
and Toxicology

Reviewed by:

Robert J. Weir, Ph.D.
Vice President

TABLES

TABLE 1

BODY WEIGHTS
(grams)

GROUP MEANS ± STANDARD ERRORS

MALES

GROUP NO.	WEEK 0	1	2	3	4	5	6	7	8	9	10	11	12	13
1 - CONTROL														
MEAN	99.5	150.8	202.6	243.7	280.8	313.5	342.7	367.4	385.0	397.6	417.2	423.0	437.6	441.5
S.E.	2.9	3.7	4.3	5.2	6.4	6.5	7.3	6.9	8.4	9.1	8.8	9.1	9.2	9.7
2 - LOW														
MEAN	99.3	153.9	197.2	255.1	295.2	330.1	356.1	380.3	403.6	414.8	438.1	441.25	459.3	466.3
S.E.	1.7	2.2	3.6	3.8	4.5	5.4	7.1	6.6	6.7	6.8	7.7	7.8	8.3	9.3
3 - MEDIUM														
MEAN	94.7	147.2	194.7	245.9	288.9	321.6	354.8	377.4	397.3	415.3	432.4	438.6	456.5	457.3
S.E.	3.0	3.6	4.9	5.5	5.6	6.4	6.6	7.2	8.2	8.8	8.9	9.0	9.4	9.6
4 - HIGH														
MEAN	100.3	150.0	201.1	251.5	291.7	326.7	354.6	374.8	400.6	415.2	434.6	442.5	456.6	460.1
S.E.	2.6	3.3	4.1	5.0	5.6	5.8	7.2	8.7	7.4	7.5	7.9	8.1	9.0	7.6

TABLE 1 (Continued)

BODY WEIGHTS
(grams)

GROUP MEANS ± STANDARD ERRORS

MALES

GROUP NO.	WEEK 14	15	16	17	18	19	20	21	22	23	24	25	26	28
1 - CONTROL														
MEAN	458.2	459.4	473.4	479.0	482.7	503.4	501.6	507.9	517.1	522.0	526.5	525.9	517.5	541.2
S.E.	10	9.9	9.7	11	11	12	12	13	12	12	12	12	12	13
2 - LOW														
MEAN	471.6	484.7	495.7	497.0	499.0	501.2	514.2	517.1	523.9	528.0	534.8	537.2	537.1	553.4
S.E.	8.5	8.4	8.6	8.9	9.6	9.1	10	9.9	9.8	10	11	11	11	11
3 - MEDIUM														
MEAN	472.0	485.9	497.2	498.0	504.5	512.0	523.5	524.3	531.9	533.0	539.4	551.1	545.9	564.8
S.E.	10	10	13	12	12	12	13	12	12	12	12	12	12	12
4 - HIGH														
MEAN	471.9	482.3	492.1	502.7	508.9	514.5	523.8	526.5	530.3	527.3	533.8	543.3	538.6	555.6
S.E.	8.5	8.9	9.3	9.9	11	10	11	11	12	12	12	12	13	12

TABLE 1 (Continued)

BODY WEIGHTS
(grams)

GROUP MEANS ± STANDARD ERRORS

GROUP NO.	WEEK 30	32	34	36	38	40	42	44	46	48	50	52	56
1 - CONTROL													
MEAN	555.8	569.8	569.9	572.7	586.8	597.5	597.5	601.7	608.7	606.8	611.3	621.9	616.1
S.E.	13	13	13	14	13	13	14	15	16	16	17	17	17
2 - LOW													
MEAN	560.3	584.4	570.2	579.9	592.1	604.7	611.9	610.6	619.0	618.5	617.3	625.6	625.3
S.E.	12	13	13	13	13	13	14	13	14	15	15	15	15
3 - MEDIUM													
MEAN	578.7	586.9	577.4	588.9	602.8	606.8	602.4	604.1	612.1	610.9	613.3	610.2	607.2
S.E.	13	12	14	14	14	15	15	16	15	16	15	15	17
4 - HIGH													
MEAN	568.5	584.6	575.6	589.7	599.9	599.6	597.2	609.1	624.8	616.1	618.8	610.2	614.0
S.E.	13	13	13	13	14	15	16	15	15	15	15	15	15

TABLE 1 (Continued)

BODY WEIGHTS
(grams)

GROUP MEANS ± STANDARD ERRORS

MALES

	WEEK												
GROUP NO.	60	64	68	72	76	80	84	88	92	94	96	100	104
1 - CONTROL													
MEAN	586.4	620.3	593.1	620.9	619.1	635.3	656.9	663.2	666.8	643.8	672.0	658.0	660.6
S.E.	17	19	17	17	15	17	16	19	18	23	19	18	21
2 - LOW													
MEAN	606.0	625.3	612.7	616.3	637.2	649.7	672.0	684.0	680.5	663.1	685.9	669.6	675.0
S.E.	15	16	13	16	15	17	18	19	21	28	23	25	28
3 - MEDIUM													
MEAN	596.6	599.8	547.9	607.2	624.5	620.6	649.1	659.4	662.8	663.4	666.3	648.5	643.0
S.E.	19	23	21	18	19	22	20	20	21	22	22	22	26
4 - HIGH													
MEAN	615.8	611.1	595.8	598.3	588.2	589.3	622.0	630.2	631.9	636.3	632.9	627.6	613.8
S.E.	15	14	13	14	17	19	18	18	21	19	20	22	32

TABLE 1 (Continued)

BODY WEIGHTS
(grams)

GROUP MEANS ± STANDARD ERRORS

FEMALES

GROUP NO.	WEEK 0	1	2	3	4	5	6	7	8	9	10	11	12	13
1 - CONTROL														
MEAN	90.2	131.3	155.2	174.0	195.2	210.2	227.0	327.5	244.8	246.1	256.1	262.5	259.7	264.8
S.E.	2.1	2.2	2.4	2.7	3.5	4.6	3.4	3.6	4.1	4.7	5.1	4.9	4.5	5.8
2 - LOW														
MEAN	87.1	128.1	154.7	170.1	189.0	204.3	216.2	228.0	236.1	241.1	248.0	251.0	254.8	257.7
S.E.	2.2	2.6	2.1	2.5	2.6	2.8	3.3	3.4	3.8	3.9	4.0	4.1	4.2	3.9
3 - MEDIUM														
MEAN	85.0	121.6	150.3	164.7	182.3	203.5	216.0	221.6	232.3	237.0	242.0	246.3	248.8	251.1
S.E.	2.3	2.6	2.8	3.7	3.3	3.1	3.3	4.1	3.8	3.5	3.5	3.9	4.0	3.9
4 - HIGH														
MEAN	89.4	124.2	151.4	173.8	193.3	203.4	217.5	231.1	238.2	245.2	253.1	252.1	260.0	260.8
A.W.	2.2	2.3	3.0	2.8	3.3	3.3	4.3	4.2	4.3	4.5	4.5	4.9	4.6	5.1

TABLE 1 (Continued)

BODY WEIGHTS
(grams)

GROUP MEANS ± STANDARD ERRORS

FEMALES

GROUP NO.	WEEK 14	15	16	17	18	19	20	21	22	23	24	25	26	28
1 - CONTROL														
MEAN	273.1	277.2	278.3	288.6	291.5	299.5	299.6	306.8	309.5	311.2	313.1	315.6	309.7	319.0
S.E.	5.3	5.1	5.5	5.6	5.7	5.9	6.2	6.3	6.6	6.5	6.7	7.1	7.3	7.6
2 - LOW														
MEAN	262.0	269.8	274.2	274.8	277.3	281.3	286.1	289.6	294.2	297.0	299.6	300.7	299.6	308.5
S.E.	4.9	5.0	4.8	4.6	4.9	4.7	5.2	5.4	5.4	5.6	5.3	5.3	5.7	6.3
3 - MEDIUM														
MEAN	256.2	264.7	268.7	270.0	273.8	277.2	280.6	280.7	283.1	285.5	287.7	292.6	291.9	298.4
S.E.	3.4	3.6	4.0	4.3	4.5	4.4	4.4	4.9	4.7	4.8	4.7	5.0	5.2	5.4
4 - HIGH														
MEAN	264.8	268.8	279.5	283.2	288.6	291.7	294.5	293.1	301.8	296.8	300.7	307.0	304.5	311.1
S.E.	5.4	5.1	5.1	5.4	5.5	5.5	5.5	5.8	6.1	6.2	6.0	6.4	6.5	6.5

TABLE 1 (Continued)

BODY WEIGHTS
(grams)

GROUP MEANS ± STANDARD ERRORS

FEMALES

GROUP NO.	WEEK 30	32	34	36	38	40	42	44	46	48	50	52	56
1 - CONTROL													
MEAN	325.1	335.4	337.5	337.3	343.8	351.8	355.5	356.1	360.1	363.4	367.7	373.7	376.7
S.E.	7.7	8.2	8.2	8.2	8.1	8.4	9.0	9.0	9.2	9.5	10	10	11
2 - LOW													
MEAN	316.4	323.3	321.7	322.4	326.9	331.8	334.8	333.5	339.8	342.1	345.0	349.7	350.7
S.E.	7.0	7.3	7.0	7.3	7.7	7.6	8.3	7.7	7.7	7.8	8.5	8.6	9.5
3 - MEDIUM													
MEAN	304.9	308.7	304.4	311.3	316.6	313.5	316.2	320.2	326.3	326.9	326.4	330.6	326.3*
S.E.	5.7	6.1	6.3	5.7	6.0	6.5	7.2	6.9	7.3	7.3	6.9	7.0	7.9
4 - HIGH													
MEAN	316.4	319.2	315.5	321.1	329.9	326.8	331.9	334.6	335.7	343.1	343.8	344.1	342.3*
S.E.	7.0	7.9	7.6	8.9	8.5	8.7	9.4	9.7	9.9	10	11	11	11

*Significantly different from Control Group ($P < 0.05$).

TABLE 1 (Continued)

BODY WEIGHTS
(grams)

GROUP MEANS ± STANDARD ERRORS

FEMALES

GROUP NO.	WEEK 60	64	68	72	76	80	84	88	92	94	96	100	104
1 - CONTROL													
MEAN	360.6	376.4	352.8	378.3	386.8	391.3	421.0	430.6	433.4	440.4	452.8	455.7	450.2
S.E.	10	12	9.0	9.9	11	12	14	17	19	21	20	20	23
2 - LOW													
MEAN	329.6*	342.0	329.7	351.8	377.3	369.7	391.8	405.1	402.8	422.8	413.5	416.5	399.4
S.E.	8.9	8.4	12	13	16	8.7	9.8	14	12	17	13	12	14
3 - MEDIUM													
MEAN	315.8*	318.0*	319.7*	328.8*	337.7*	340.6*	361.2*	364.5*	375.3*	378.8*	374.3*	378.7*	368.5*
S.E.	8.3	7.3	6.9	6.3	6.7	8.7	9.9	11	11	12	13	14	17
4 - HIGH													
MEAN	334.9*	341.7	318.4*	344.9*	345.9	354.0*	372.9*	377.6*	385.0	398.6	404.8	397.5	408.2
S.E.	11	13	11	11	12	12	14	16	17	18	18	21	20

*Significantly different from Control Group ($P < 0.05$).

TABLE 2

FOOD CONSUMPTION
(grams/day)

GROUP MEANS ± STANDARD ERRORS

MALES

	WEEK													
GROUP NO.	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1 - CONTROL														
MEAN	18.5	22.2	25.5	29.2	29.0	28.2	26.9	26.7	29.0	26.6	25.7	25.6	22.6	26.3
S.E.	0.3	0.5	0.9	1.2	1.0	0.9	1.0	1.0	1.0	0.8	0.8	0.5	0.8	0.9
2 - LOW														
MEAN	18.8	21.1	25.5	28.0	28.2	30.5	26.9	27.3	28.7	27.2	27.1	26.0	22.8	25.8
S.E.	0.5	0.5	0.6	0.8	0.8	1.0	0.7	0.8	0.7	0.7	0.7	0.6	0.5	0.6
3 - MEDIUM														
MEAN	18.2	21.8	24.4	28.6	27.8	27.8	27.5	28.1	26.8	26.7	24.9	26.3	23.2	26.5
S.E.	0.4	0.5	0.7	0.6	0.6	0.6	0.5	0.6	0.5	0.6	0.5	0.5	0.4	0.5
4 - HIGH														
MEAN	19.0	22.3	25.1	29.5	28.5	29.9	27.0	28.1	29.9	28.7	28.9	27.8	24.7	26.6
S.E.	0.4	0.5	0.6	0.9	0.6	0.8	0.6	0.5	0.9	0.7	0.9	0.9	0.6	0.5

TABLE 2 (Continued)

FOOD CONSUMPTION
(grams/day)

GROUP MEANS ± STANDARD ERRORS

MALES

GROUP NO.	WEEK 15	16	17	18	19	20	21	22	23	24	25	26	28
1 - CONTROL													
MEAN	27.7	28.1	25.6	24.9	25.5	26.0	25.1	25.0	23.7	25.5	22.8	23.4	27.6
S.E.	0.5	0.9	0.8	0.7	0.7	0.9	0.7	0.5	0.6	0.6	0.5	0.7	0.5
2 - LOW													
MEAN	27.7	29.5	26.5	25.6	25.2	26.1	25.9	25.3	24.9	25.7	24.5	24.9	27.6
S.E.	0.7	1.0	0.7	0.5	0.6	1.0	0.8	0.7	0.8	0.6	0.8	0.7	0.9
3 - MEDIUM													
MEAN	28.0	31.4	27.1	26.1	25.1	27.9	25.3	27.2	27.0	27.2	25.4	24.8	28.9
S.E.	0.8	1.3	1.4	0.6	0.7	0.8	0.5	0.6	0.8	0.7	0.6	0.7	0.7
4 - HIGH													
MEAN	26.6	27.6	27.9	28.2	26.6	27.4	24.5	26.5	25.3	26.5	24.8	25.2	27.9
S.E.	0.6	0.8	0.9	0.8	0.5	1.2	0.6	0.7	0.7	0.6	0.8	0.8	0.8

TABLE 2 (Continued)

FOOD CONSUMPTION
(grams/day)

GROUP MEANS ± STANDARD ERRORS

MALES

	WEEK												
GROUP NO.	30	32	34	36	38	40	42	44	46	48	50	52	56
1 - CONTROL													
MEAN	25.1	25.3	23.4	22.1	21.7	20.8	20.0	22.2	22.6	22.6	23.4	23.3	22.8
S.E.	0.5	0.5	0.6	0.4	0.4	0.3	0.4	0.5	0.5	0.4	0.5	0.5	0.5
2 - LOW													
MEAN	26.6	25.7	25.3	22.3	21.8	22.1	21.0	23.6	21.5	22.8	21.9	22.6	22.7
S.E.	0.9	0.5	1.2	0.4	0.5	0.4	0.6	0.4	0.5	0.4	0.4	0.4	0.5
3 - MEDIUM													
MEAN	28.3	26.0	25.0	23.2	21.5	23.2	21.5	24.0	22.6	23.6	22.9	24.0	24.3
S.E.	0.9	0.9	1.1	0.5	0.5	0.5	0.8	0.7	0.7	0.9	0.4	0.6	0.7
4 - HIGH													
MEAN	26.0	27.8	23.7	22.4	22.2	22.9	21.8	23.9	23.0	23.0	23.1	23.1	24.2
S.E.	0.7	0.8	1.0	0.8	0.7	1.1	0.8	0.6	0.5	0.4	0.5	0.6	0.6

TABLE 2 (Continued)

FOOD CONSUMPTION
(grams/day)

GROUP MEANS ± STANDARD ERRORS

MALES

GROUP NO.	WEEK 60	64	68	72	76	80	84	88	92	94	96	100	104
1 - CONTROL													
MEAN	27.6	22.9	22.6	25.7	24.6	25.8	22.0	22.0	20.8	21.1	22.4	23.0	22.3
S.E.	0.9	0.5	0.6	0.5	0.5	1.1	0.7	0.5	0.4	0.4	0.5	0.4	0.6
2 - LOW													
MEAN	26.4	21.5	21.3	25.0	25.0	24.0	22.8	22.3	21.2	21.8	22.4	22.7	21.6
S.E.	0.6	0.7	0.5	0.5	0.4	0.6	0.6	0.6	0.6	0.7	0.9	0.9	1.1
3 - MEDIUM													
MEAN	25.7	20.1*	25.4*	25.4	24.5	23.4	27.0*	23.8*	23.0*	22.5	22.0	23.1	21.7
S.E.	0.7	0.7	0.6	0.6	0.7	0.7	2.2	0.6	0.6	0.8	0.8	0.7	1.1
4 - HIGH													
MEAN	24.2*	22.1	22.2	24.8	24.0	24.0	23.3	22.7	22.5*	21.1	22.1	23.5	20.2
S.E.	0.6	0.5	0.5	0.4	0.8	0.9	0.9	0.7	0.6	0.6	0.8	0.6	1.1

*Significantly different from Control Group ($P < 0.05$).

TABLE 2 (Continued)

FOOD CONSUMPTION
(grams/day)

GROUP MEANS ± STANDARD ERRORS

FEMALES

GROUP NO.	WEEK 1	2	3	4	5	6	7	8	9	10	11	12	13	14
1 - CONTROL														
MEAN	17.3	20.5	20.9	23.5	23.7	21.0	19.8	22.1	24.4	21.1	21.5	19.5	17.0	20.6
S.E.	0.3	0.3	0.9	1.1	1.0	0.8	0.6	1.0	1.2	0.8	0.8	0.5	0.9	0.9
2 - LOW														
MEAN	16.3	17.8	21.4	23.0	23.6	23.6	21.4	23.1	23.5	23.0	22.5	18.9	17.2	21.5
S.E.	0.8	0.7	1.4	1.1	1.4	1.3	1.2	1.2	1.2	1.2	1.1	0.8	1.0	1.1
3 - MEDIUM														
MEAN	16.6	17.5	19.8	24.0	21.1	23.0	20.2	22.4	22.7	22.5	20.9	17.7	16.4	18.4
S.E.	0.5	0.7	1.1	1.3	1.1	1.3	0.8	1.2	1.4	1.1	1.3	0.8	0.7	1.0
4 - HIGH														
MEAN	16.0	17.8	21.0	25.0	24.1	24.9	23.2	24.2	25.1	23.0	23.5	21.0	18.3	20.7
S.E.	0.4	0.4	1.2	1.5	1.3	1.4	1.3	1.2	1.4	1.1	1.5	1.1	1.2	1.2

TABLE 2 (Continued)

FOOD CONSUMPTION
(grams/day)

GROUP MEANS ± STANDARD ERRORS

FEMALES

GROUP NO.	WEEK 15	16	17	18	19	20	21	22	23	24	25	26	28
1 - CONTROL													
MEAN	22.1	23.7	20.0	20.8	20.2	20.0	19.1	19.3	18.9	19.0	18.4	17.6	21.0
S.E.	0.8	0.8	0.6	1.0	0.9	0.7	0.6	0.6	0.6	0.6	0.6	0.4	0.7
2 - LOW													
MEAN	22.9	25.8	20.9	20.4	19.6	20.3	18.6	19.1	19.4	20.0	17.9	18.0	20.9
S.E.	1.0	1.1	1.0	0.7	0.8	0.5	0.6	0.6	0.5	0.9	0.7	0.5	0.7
3 - MEDIUM													
MEAN	20.6	22.9	21.5	20.9	20.5	20.6	18.1	20.2	19.3	20.2	19.0	18.3	20.1
S.E.	0.8	1.0	1.2	1.3	1.1	0.8	0.7	1.0	0.6	1.0	0.8	0.7	0.6
4 - HIGH													
MEAN	21.1	22.2	21.3	20.7	19.5	20.7	19.9	21.0	20.1	20.2	18.6	18.4	21.1
S.E.	0.9	1.2	1.0	0.9	0.8	0.7	1.7	0.9	0.6	0.8	0.7	0.7	1.1

TABLE 2 (Continued)

FOOD CONSUMPTION
(grams/day)

GROUP MEANS ± STANDARD ERRORS

FEMALES

GROUP NO.	WEEK 30	32	34	36	38	40	42	44	46	48	50	52	56
1 - CONTROL													
MEAN	19.0	18.6	17.3	15.7	15.9	15.4	16.0	16.2	17.4	18.5	17.9	17.9	18.2
S.E.	0.5	0.5	0.8	0.5	0.5	0.6	0.6	0.5	0.4	0.5	0.7	0.5	0.7
2 - LOW													
MEAN	20.7	18.3	18.2	16.1	15.8	15.4	16.0	16.6	17.2	18.6	17.4	17.9	17.6
S.E.	1.0	0.6	0.6	0.5	0.4	0.4	0.5	0.5	0.5	0.5	0.6	0.6	0.8
3 - MEDIUM													
MEAN	19.5	16.9	17.7	15.5	15.0	15.3	15.5	16.6	16.3	17.8	17.2	17.4	18.5
S.E.	0.7	0.5	1.0	0.4	0.3	0.6	0.4	0.4	0.5	1.0	0.8	0.5	0.8
4 - HIGH													
MEAN	20.1	19.7	18.0	17.1	16.6	15.7	16.3	17.3	16.9	17.0	17.2	17.9	18.3
S.E.	1.2	0.9	0.8	0.7	0.7	0.6	0.6	0.6	0.6	0.6	0.6	0.7	0.6

TABLE 2 (Continued)

FOOD CONSUMPTION
(grams/day)

GROUP MEANS ± STANDARD ERRORS

FEMALES

	WEEK												
GROUP NO.	60	64	68	72	76	80	84	88	92	94	96	100	104
1 - CONTROL													
MEAN	23.2	17.7	18.8	21.6	19.4	21.4	18.2	18.4	16.7	17.2	17.6	18.8	17.4
S.E.	0.7	0.6	0.7	0.7	0.5	0.9	0.4	0.5	0.6	0.6	0.6	0.6	0.5
2 - LOW													
MEAN	21.8	15.8*	15.4*	20.3	20.0	19.3	17.4	18.0	17.4	18.5	18.4	18.6	16.4
S.E.	0.7	0.6	0.6	0.6	0.7	0.8	0.6	0.6	0.6	0.8	0.6	0.6	0.9
3 - MEDIUM													
MEAN	20.8*	15.1*	15.6*	19.7*	19.2	19.0*	17.9	17.0	15.8	16.7	16.6	18.4	17.5
S.E.	0.7	0.6	0.6	0.4	0.5	0.7	0.6	0.6	0.5	0.6	0.6	1.0	0.8
4 - HIGH													
MEAN	20.6*	16.0	19.7	20.0	19.5	19.2	17.9	17.8	16.9	18.1	16.7	18.8	16.4
S.E.	0.9	0.7	0.9	0.8	0.6	0.7	0.8	0.9	0.9	0.8	0.7	0.7	0.7

*Significantly different from Control Group ($P < 0.05$).

TABLE 3

HEMATOCYTOLOGY

GROUP MEANS ± STANDARD ERROR

MALES

GROUP NO.	RBC/mm^3 (x 10^6)	RETIC. %	CELL VOL. %	HEMO-GLOBIN gm %	WBC/mm^3 (x 10^3)	DIFFERENTIAL (%)* Ban	Seg	Ly	Mo	Eo
				13-WEEKS						
1 - CONTROL										
MEAN	8.37	1.9	43.9	14.7	13.7	<1	20	79	<1	1
S.E.	0.29	0.30	0.92	0.29	1.1	-	3.0	3.2	-	-
2 - LOW										
MEAN	8.62	0.4**	47.5**	15.8**	14.7	0	11	68	<1	2
S.E.	0.16	0.10	0.56	0.18	0.47		2.0	1.9	-	0.37
3 - MEDIUM										
MEAN	8.59	2.1	43.8	14.7	15.2	0	25	73	1	1
S.E.	0.26	0.17	1.5	0.49	0.87		1.9	1.9	-	-
4 - HIGH										
MEAN	8.41	1.3	45.9	15.2	13.9	0	13	84	<1	2
S.E.	0.30	0.40	1.15	0.32	0.68		2.0	2.2	-	0.46

*Ban - Bands; Seg - Segmented Neutrophils; Ly - Lymphocytes; Mo - Monocytes; Eo - Eosinophils.
**Significantly different from control group ($p < 0.05$).

TABLE 3 (Continued)

HEMATOCYTOLOGY

GROUP MEANS ± STANDARD ERROR

MALES

GROUP NO.	RBC/mm^3 (x 10^6)	RETIC. %	CELL VOL. %	HEMO-GLOBIN gm %	WBC/mm^3 (x 10^3)	DIFFERENTIAL (%)* Ban	Seg	Ly	Mo	Eo
				26-WEEKS						
1 - CONTROL										
MEAN	8.99	1.6	45.0	15.0	11.0	0	14	84	1	1
S.E.	0.17	0.37	0.39	0.15	1.1		2.9	3.0	-	-
(N=9)										
2 - LOW										
MEAN	9.31	3.0**	46.5**	15.4	12.7	0	23	74	1	2
S.E.	0.19	0.35	0.50	0.20	0.56		2.9	3.0	-	0.43
3 - MEDIUM										
MEAN	9.26	1.4	47.0**	15.2	13.8	0	19	80	1	1
S.E.	0.13	0.17	0.31	0.14	0.93		2.3	2.3	-	-
4 - HIGH										
MEAN	8.33**	1.9	45.4	15.1	12.9	<1	21	77	1	2
S.E.	0.21	0.26	0.53	0.17	0.65	-	2.5	2.5	-	0.63

*Ban - Bands; Seg - Segmented Neutrophils; Ly - Lymphocytes; Mo - Monocytes; Eo - Eosinophils.
**Significantly different from control group ($p < 0.05$).
Number of animals per group (N) is 10 except where otherwise noted.

TABLE 3 (Continued)

HEMATOCYTOLOGY

GROUP MEANS ± STANDARD ERROR

MALES

GROUP NO.	RBC/mm^3 (x 10^6)	RETIC. %	CELL VOL. %	HEMO-GLOBIN gm %	WBC/mm^3 (x 10^3)	DIFFERENTIAL (%)* Ban	Seg	Ly	Mo	Eo
				52-WEEKS						
1 - CONTROL										
MEAN	7.51	2.7	44.5	15.5	12.4	<1	22	76	1	1
S.E.	0.18	0.26	0.76	0.23	0.97	-	2.5	2.7	-	-
2 - LOW										
MEAN	7.41	2.4	44.0	15.1	12.6	0	18	81	<1	1
S.E.	0.24	0.30	0.68	0.24	0.58		3.2	3.3	-	-
3 - MEDIUM										
MEAN	7.30	2.9	43.5	15.1	14.2	0	19	79	1	1
S.E.	0.18	0.58	0.70	0.23	1.1		2.4	2.7	-	-
4 - HIGH										
MEAN	7.36	2.5	43.5	15.0	14.1	0	20	77	1	1
S.E.	0.31	0.31	1.2	0.48	0.68		2.2	2.3	-	-

*Ban - Bands; Seg - Segmented Neutrophils; Ly - Lymphocytes; Mo - Monocytes; Eo - Eosinophils.

TABLE 3 (Continued)

HEMATOCYTOLOGY

GROUP MEANS ± STANDARD ERROR

MALES

GROUP NO.	RBC/mm³ (x 10⁶)	RETIC. %	CELL VOL. %	HEMO-GLOBIN gm %	WBC/mm³ (x 10³)	DIFFERENTIAL (%)* Ban	Seg	Ly	Mo	Eo
				104-WEEKS						
1 - CONTROL										
MEAN	7.68	0.2	42.5	13.9	10.2	0	32	65	2	2
S.E.	0.32	0.033	0.76	0.49	0.59	0.11	2.1	2.2	0.95	0.32
2 - LOW										
MEAN	7.91	0.7	41.3	14.3	8.9	0	28	70	-	2
S.E.	0.50	0.31	0.86	0.29	1.0	0	3.2	3.3	-	0.33
3 - MEDIUM										
MEAN	8.18	1.2**	43.5	14.5	8.0**	0	36	60	1	2
S.E.	0.22	0.23	0.76	0.30	0.70	0	4.9	4.9	0.38	0.48
4 - HIGH										
MEAN	7.55	1.9**	40.0**	13.9	6.7**	0	33	62	1	4
S.E.	0.24	0.31	0.84	0.29	0.34	0.11	3.0	2.9	0.47	0.82

*Ban - Bands; Seg - Segmented Neutrophils; Ly - Lymphocytes; Mo - Monocytes; Eo - Eosinophils.
**Significantly different from control group ($p<0.05$).

TABLE 3 (Continued)

HEMATOCYTOLOGY

GROUP MEANS ± STANDARD ERROR

FEMALES

GROUP NO.	RBC/mm^3 (x 10^6)	RETIC. %	CELL VOL. %	HEMO-GLOBIN gm %	WBC/mm^3 (x 10^3)	DIFFERENTIAL (%)* Ban	Seg	Ly	Mo	Eo
				13-WEEKS						
1 - CONTROL										
MEAN	7.29	1.1	39.6	13.6	10.4	0	16	82	1	1
S.E.	0.39	0.37	1.0	0.37	0.70		3.1	3.0	-	-
2 - LOW										
MEAN	8.39**	0.1**	46.1**	15.8**	10.1	0	10	89	<1	1
S.E.	0.16	0.024	0.44	0.18	0.71		1.3	1.3	-	-
3 - MEDIUM										
MEAN	8.55	2.2**	43.2	15.0	11.7	<1	14	84	1	1
S.E.	0.60	0.38	3.3	1.1	1.4	-	2.8	3.2	-	-
4 - HIGH										
MEAN	6.87	0.1**	43.5	14.6	13.6**	<1	11	87	<1	2
S.E.	0.30	0.023	1.7	0.58	0.46		2.0	2.1	-	0.45

*Ban - Bands; Seg - Segmented Neutrophils; Ly - Lymphocytes; Mo - Monocytes; Eo - Eosinophils.
**Significantly different from control group ($p < 0.05$).

TABLE 3 (Continued)

HEMATOCYTOLOGY

GROUP MEANS ± STANDARD ERROR

FEMALES

GROUP NO.	RBC/mm^3 (x 10^6)	RETIC %	CELL VOL. %	HEMO-GLOBIN gm %	WBC/mm^3 (x 10^3)	DIFFERENTIAL (%)* Ban	Seg	Ly	Mo	Eo
				26-WEEKS						
1 - CONTROL										
MEAN	7.63	3.4	42.5	14.3	9.5	0	10	88	<1	1
S.E.	0.19	1.1	0.43	0.14	0.87		1.3	1.7	-	-
2 - LOW										
MEAN	8.67**	2.6	45.5**	15.1**	8.1	0	15	83	1	1
S.E.	0.14	0.33	0.51	0.19	0.72		2.1	2.2	-	-
3 - MEDIUM										
MEAN	8.70**	1.3	45.0**	14.9	7.6	0	20	78	1	2
S.E.	0.18	0.13	0.62	0.27	1.25		4.1	4.3	-	0.56
4 - HIGH										
MEAN	7.90	2.4	46.0**	15.6**	10.3	0	14	84	1	2
S.E.	0.26	0.54	0.52	0.13	0.75		1.4	1.6	-	0.33

*Ban - Bands; Seg - Segmented Neutrophils; Ly - Lymphocytes; Mo - Monocytes; Eo - Eosinophils.
**Significantly different from control group ($p < 0.05$).

TABLE 3 (Continued)

HEMATOCYTOLOGY

GROUP MEANS ± STANDARD ERROR

FEMALES

GROUP NO.	RBC/mm^3 (x 10^6)	RETIC %	CELL VOL. %	HEMO-GLOBIN gm %	WBC/mm^3 (x 10^3)	DIFFERENTIAL (%)* Ban	Seg	Ly	Mo	Eo
				52-WEEKS						
1 - CONTROL										
MEAN	6.90	2.4	44.0	15.3	10.0	<1	21	77	<1	1
S.E.	0.20	0.36	0.68	0.17	0.91	-	3.2	3.4	-	-
2 - LOW										
MEAN	6.72	2.7	42.0**	14.7**	11.9	0	25	73	1	1
S.E.	0.24	0.31	0.68	0.22	0.84		4.1	4.3	-	-
3 - MEDIUM										
MEAN	7.12	2.5	43.0	15.3	12.0	0	20	78	1	1
S.E.	0.15	0.31	0.61	0.22	1.3		4.6	4.6	-	-
4 - HIGH										
MEAN	6.95	3.2	43.5	15.3	10.9	0	20	77	1	2
S.E.	0.24	0.54	0.58	0.26	0.93		2.9	3.4	-	0.57

*Ban - Bands; Seg - Segmented Neutrophils; Ly - Lymphocytes; Mo - Monocytes; Eo - Eosinophils.
**Significantly different from control group ($p < 0.05$).

TABLE 3 (Continued)

HEMATOCYTOLOGY

GROUP MEANS ± STANDARD ERROR

FEMALES

GROUP NO.	RBC/mm^3 (x 10^6)	RETIC. %	CELL VOL. %	HEMO-GLOBIN gm %	WBC/mm^3 (x 10^3)	DIFFERENTIAL (%)* Ban	Seg	Ly	Mo	Eo
				104-WEEKS						
1 - CONTROL										
MEAN	6.75	0.5	39.0	13.4	8.1	0	33	65	0.4	2
S.E.	0.20	0.11	0.77	0.32	0.76	0	4.3	4.2	0.22	0.37
2 - LOW										
MEAN	5.79	1.4**	37.8	13.2	8.5	0	39	58	0	2
S.E.	0.71	0.29	0.64	0.22	0.76	0	2.6	3.0	0.15	0.59
3 - MEDIUM										
MEAN	7.20	0.3	39.5	13.6	5.5**	0	34	64	1	1
S.E.	0.21	0.11	1.0	0.37	0.71	0	3.5	3.4	0.37	0.22
4 - HIGH										
MEAN	6.89	0.6	38.5	13.1	7.1	0	43	54	1	2
S.E.	0.12	0.23	0.45	0.18	0.50	0	2.3	2.4	0.28	0.53

*Ban - Bands; Seg - Segmented Neutrophils; Ly - Lymphocytes; Mo - Monocytes; Eo - Eosinophils.
**Significantly different from control group ($p<0.05$).

TABLE 4

BLOOD CHEMISTRY

GROUP MEANS ± STANDARD ERROR

MALES

GROUP NO.	GLUCOSE mg %	BUN mg %	Na mEq/L	K mEq/L	Cl mEq/L	ALK. PHOS. I.U.	SGOT I.U.	SGPT I.U.	TOTAL BILIRUBIN mg %	TOTAL PROTEIN gm %	METHGB. % Sat.
					52-WEEKS						
1 - CONTROL											
MEAN	146	12.4	145	5.7	101	15.1	164	19.9	0.20	6.5	3.7
S.E.	4.0	0.46	0.56	0.07	0.69	0.70	17	1.5	0.047	0.11	1.4
2 - LOW											
MEAN	155	12.7	144	5.9	102	17.9	180	25.8*	0.09*	6.7	5.3
S.E.	6.7	0.53	0.83	0.25	0.86	2.7	10	2.3	0.018	0.12	1.3
3 - MEDIUM											
MEAN	137	14.7	145	5.9	101	18.1	183	23.0	0.12	6.5	8.5*
S.E.	5.7	1.8	0.37	0.24	0.69	3.0	7.6	1.4	0.039	0.15	1.8
4 - HIGH											
MEAN	137	12.6	145	5.9	101	17.4	168	19.0	0.12	6.6	2.2
S.E.	3.1	0.60	0.81	0.20	0.72	1.1	13	1.0	0.026	0.15	0.85

*Significantly different from control group ($p < 0.05$).

TABLE 4 (Continued)

BLOOD CHEMISTRY

GROUP MEANS ± STANDARD ERROR

MALES

GROUP NO.	GLUCOSE mg %	BUN mg %	Na mEq/L	K mEq/L	Cl mEq/L	ALK. PHOS. I.U.	SGOT I.U.	SGPT I.U.	TOTAL BILIRUBIN mg %	TOTAL PROTEIN gm %	MET-* HGB. % Sat.
					104-WEEKS						
1 - CONTROL											
MEAN	165	19	145	5.2	107	13.4	189	31	0.3	6.0	3.4
S.E.	8.7	2.2	0.49	0.12	0.59	2.1	28	5.1	0.057	0.11	0.77
2 - LOW											
MEAN	135	18	148**	5.7	107	11.3	247	34	0.3	6.1	6.4**
S.E.	13	2.4	0.86	0.33	0.87	1.8	22	4.4	0.038	0.12	0.18
3 - MEDIUM											
MEAN	141	17	150**	6.6**	110**	9.4	325**	61**	0.4	6.4**	2.2
S.E.	11	1.7	0.73	0.20	0.47	0.52	21	11	0.038	0.17	0.83
4 - HIGH											
MEAN	153	18	149**	6.4**	111**	9.4	161	38	0.5**	5.8	4.2
S.E.	7.9	2.5	0.66	0.46	0.77	0.53	14	4.2	0.06	0.15	1.3

*Determinations made on different rats.
**Significantly different from control group ($p<0.05$).

TABLE 4 (Continued)

BLOOD CHEMISTRY

GROUP MEANS ± STANDARD ERROR

FEMALES

GROUP NO.	GLUCOSE mg %	BUN mg %	Na mEq/L	K mEq/L	Cl mEq/L	ALK. PHOS. I.U.	SGOT I.U.	SGPT I.U.	TOTAL BILIRUBIN mg %	TOTAL PROTEIN gm %	MET-HGB. % Sat.
					52-WEEKS						
1 - CONTROL											
MEAN	157	13.3	143	5.0	97	8.7	112	20.5	0.20	7.0	4.0
S.E.	3.2	0.47	0.70	0.18	0.87	0.54	8.2	1.3	0.057	0.10	1.2
2 - LOW											
MEAN	147	12.4	144	4.8	98	8.8	145*	22.9	0.13	6.9	6.5
S.E.	4.7	0.68	0.89	0.15	0.77	0.71	7.5	1.8	0.021	0.060	1.9
3 - MEDIUM											
MEAN	147	11.9	144	5.1	99	11.4	138*	21.2	0.16	7.0	8.5*
S.E. (N=9)	4.1	0.69	0.38	0.28	0.93	1.3	10	1.8	0.037	0.17	1.8
4 - HIGH											
MEAN	136*	12.7	144	5.0	100*	7.8	143	23.5	0.08	6.8	2.2
S.E. (N=6)	4.3	0.39	0.83	0.15	0.99	0.55	19	3.0	0.017	0.16	1.04

*Significantly different from control group ($p < 0.05$).
Number of animals per group (N) is 10 except where otherwise noted.

TABLE 4 (Continued)

BLOOD CHEMISTRY

GROUP MEANS ± STANDARD ERROR

FEMALES

GROUP NO.	GLUCOSE mg %	BUN mg %	Na mEq/L	K mEq/L	Cl mEq/L	ALK. PHOS. I.U.	SGOT I.U.	SGPT I.U.	TOTAL BILIRUBIN mg %	TOTAL PROTEIN gm %	MET-* HGB. % Sat.
					104-WEEKS						
1 - CONTROL											
MEAN	136	16	143	4.7	104	6.9	231	38	0.3	7.0	3.1
S.E.	9.0	1.4	0.60	0.16	1.3	0.24	29	6.5	0.048	0.12	0.98
2 - LOW											
MEAN	136	18	147**	5.6**	106	7.1	217	25	0.5**	6.8	2.7
S.E.	7.1	2.0	0.71	0.34	1.3	0.72	16	3.4	0.066	0.22	0.71
3 - MEDIUM											
MEAN	139	14	148**	5.1	109**	5.9**	242	36	0.4	6.8	3.9
S.E.	4.4	0.82	0.67	0.17	1.1	0.29	21	4.1	0.054	0.16	1.1
4 - HIGH											
MEAN	139	17	148**	4.6	109**	6.9	212	30	0.4	7.4**	-
S.E.	5.8	1.2	0.42	0.20	1.4	0.28	27	4.9	0.060	0.14	-

*Determinations made on different rats.
**Significantly different from control group ($p<0.05$).

TABLE 5

URINALYSIS

KEY TO ABBREVIATIONS AND SYMBOLS

Color:	Y = Yellow
	Str = Straw
	Bei = Beige
	Crm = Cream
	YBr = Yellow Brown
	Br = Brown
Appearance:	Cldy = Cloudy
	Sl Cldy = Slightly Cloudy
Albumin:	0 = Negative
	+ = Trace
	1+ = 30 mg
	2+ = 100 mg
	3+ = 300 mg
	4+ = 1000 mg or greater
Other:	- or 0 = None seen or Negative
	+ = Trace, Rare, Occasional
	1+ = Slight, Small, Little
	2+ = Moderate, Frequent
	3+ = Severe, Heavy, Large, Many
	4+ = Maximal
WBC:	cl = With clumps
Epithelial Cells:	sq = Squamous
Casts:	fgr = Finely Granular
	cgr = Coarsely Granular
	WBC = White Blood Count (Leukocyte)
	hy = Hyaline
	P = Pus
Crystals:	U.A. = Uric Acid
	T.P. = Triple Phosphate
	CA.OX = Calcium Oxalate
	LEU = Leucine
	SU = Sulfa
Other:	Yst = Yeast
	Mu = Mucous Threads
	Sp = Sperm

TABLE 5

URINALYSIS - POOLED SAMPLES

13-WEEKS

GROUP NO. & DOSE LEVEL	SEX	SPEC. GRAV.	pH	GLU-COSE	KE-TONES	BILI-RUBIN	UGOT	MICROSCOPIC EXAMINATION/HPF*						
								RBC	WBC	EPITH	BACT	AMORPH	CRYSTALS** U.A.	CRYSTALS** T.P.
1 - CONTROL	M	1.027	6.0	0	0	0	52	2-3	6-8	±	2+	1+	±	-
1 - CONTROL	F	1.027	7.0	0	0	0	34	0-1	10-12	-	2+	1+	-	±
2 - LOW	M	1.049	6.0	0†	1+	0	82	15-20	12-14 cl	±	-	3+	-	-
2 - LOW	F	1.026	6.0	0	0	0	24	-	8-10	-	±	1+	-	-
3 - MEDIUM	M	1.019	7.0	0	0	0	40	10-25	1-5	0-3	2+	1+	-	±
3 - MEDIUM	F	1.015	7.0	0	0	0	15	±	-	0-2	1+	1+	-	-
4 - HIGH	M	1.042	6.0	0	0	0	58	±	1-3	0-2	-	1+	-	3-10
4 - HIGH	F	1.013	7.0	0	0	0	17	-	0-2	0-1	2+	2+	-	0-2

*Microscopic (Per High Power Field).
**Crystals: U.A. - Uric Acid; T.P. - Triple Phosphate.
†Positive for non-glucose reducing substances.

TABLE 5 (Continued)

URINALYSIS - POOLED SAMPLES

26-WEEKS

GROUP NO. & DOSE LEVEL	SEX	SPEC. GRAV.	pH	GLU-COSE	KE-TONES	BILI-RUBIN	UGOT	MICROSCOPIC EXAMINATION/HPF*						
								RBC	WBC	EPITH	BACT	AMORPH	CRYSTALS** U.A.	CRYSTALS** T.P.
1 - CONTROL	M	1.015	7.0	0	0	0	15	-	2-4	-	±	1+	±	2+
1 - CONTROL	F	1.015	6.5	0	0	0	8	-	1-3	±	±	1+	-	-
2 - LOW	M	1.016	7.0	0	0	0	7	8-10	1-4	-	±	1+	±	±
2 - LOW	F	1.020	6.5	0	0	0	8	-	1-3	-	±	1+	±	-
3 - MEDIUM	M	1.024	7.0	0	0	0	10	4-6	0-2	-	±	1+	±	-
3 - MEDIUM	F	1.016	7.0	0	0	0	37	-	2-5	±	±	-	±	±
4 - HIGH	M	1.033	6.5	0	0	0	8	2-4	0-2	-	1+	1+	2+	-
4 - HIGH	F	1.021	6.0	0	0	0	32	-	1-3	±	1+	1+	±	-

*Microscopic (Per High Power Field).
**Crystals: U.A. - Uric Acid; T.P. - Triple Phosphate.

TABLE 5 (Continued)

URINALYSIS - POOLED SAMPLES

52-WEEKS

GROUP NO. & DOSE LEVEL	SEX	SPEC. GRAV.	pH	GLU-COSE	KE-TONES	BILI-RUBIN	UGOT	MICROSCOPIC EXAMINATION/HPF*						
								RBC	WBC	EPITH	BACT	AMORPH	CRYSTALS** U.A.	CRYSTALS** T.P.
1 - CONTROL	M	1.023	7.0	0	0	0	23	-	0-2	-	3+	2+	-	1+
1 - CONTROL	F	1.013	7.0	0	0	0	15	-	0-2	-	3+	1+	-	1+
2 - LOW	M	1.015	7.0	0	0	0	16	-	0-2	-	3+	1+	-	-
2 - LOW	F	1.014	7.5	0	0	0	32	1-4	-	sq ±	3+	1+	-	1+
3 - MEDIUM	M	1.027	7.0	0	0	0	44	-	0-2	±	1+	1+	-	3+
3 - MEDIUM	F	1.018	7.0	0	0	0	38	-	0-1	-	1+	1+	-	±
4 - HIGH	M	1.040	7.0	0	0	0	22	1-8	0-2	±	1+	1+	-	3+
4 - HIGH	F	1.020	7.0	0	0	0	33	2-6	0-1	±	1+	1+	-	3+

*Microscopic (Per High Power Field).
**Crystals: U.A. - Uric Acid; T.P. - Triple Phosphate.

TABLE 5 (Continued)

URINALYSIS - POOLED SAMPLES

104-WEEKS

GROUP NO. & DOSE LEVEL	SEX	SPEC. GRAV.	pH	GLUCOSE	KETONES	BILIRUBIN	UGOT	MICROSCOPIC EXAMINATION/HPF*						
								RBC	WBC	EPITH	BACT	AMORPH	CRYSTALS** U.A.	CRYSTALS** T.P.
1 - CONTROL	M	1.018	7.0	3+	0	0	26	2-5	0-1	-	2+	2+	-	1+
1 - CONTROL	F	1.016	6.5	0	0	0	30	±	0-2	-	2+	2+	1+	-
2 - LOW	M	1.022	8.0	0	0	0	20	18-20	±	-	1+	1+	-	-
2 - LOW	F	1.015	6.0	0	0	0	13	12-16	4-6	-	3+	2+	1+	-
3 - MEDIUM	M	1.013	7.0	0	0	0	8	21-26	8-10	2-6	2+	1+	-	-
3 - MEDIUM	F	1.013	6.0	0	0	0	5	20-25	2-4	1-3	2+	1+	1+	-
4 - HIGH	M	1.019	8.0	0	0	0	22	1-3	0-1	1-2	2+	2+	-	3+
4 - HIGH	F	1.016	8.0	0	0	0	70	-	1-4	2-3	2+	2+	-	3+

*Microscopic (Per High Power Field).
**Crystals: U.A. - Uric Acid; T.P. - Triple Phosphate.

TABLE 6

ORGAN WEIGHTS
(grams)

52-WEEK SACRIFICE - MALES

GROUP 1 - CONTROL

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
4772	658.0	0.0230	1.4020	14.7600	0.7200	4.0960	0.0510	5.6100
4775	670.0	0.0240	1.6840	14.8150	0.8840	3.8060	0.0700	6.0360
4781	529.0	0.0260	1.5990	13.0090	0.6740	3.5150	0.0510	3.8890
4784	712.0	0.0270	1.7990	14.1500	1.2080	3.5710	0.0610	6.2490
4787	627.0	0.0280	1.5570	13.5000	0.7640	3.2130	0.0510	6.3200
4790	574.0	0.0260	1.4600	13.1890	0.8360	3.2160	0.0660	4.5850
4793	608.0	0.0300	1.5740	14.6400	0.8040	4.2060	0.0500	5.1940
4796	645.0	0.0320	1.7750	17.6680	1.1670	3.7990	0.0690	5.6050
4799	589.0	0.0270	1.7410	16.0570	0.6520	4.1820	0.0580	4.4240
4802	655.0	0.0320	1.8570	17.7230	1.1050	4.3370	0.0640	6.1670
N	10	10	10	10	10	10	10	10
MEAN	626.7	0.0275	1.6456	14.9511	0.8814	3.7941	0.0591	5.4079
S.D.	53.1	0.0031	0.1596	1.7018	0.2060	0.4090	0.0080	0.8556
S.E.	16.8	0.0010	0.0476	0.5381	0.0651	0.1293	0.0025	0.2706

TABLE 6 (Continued)

ORGAN WEIGHTS
(grams)

52-WEEK SACRIFICE - MALES

GROUP 2 - LOW

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
4922	602.0	0.0180	1.7000	13.8490	0.7410	3.9390	0.0450	5.1020
4928	724.0	0.0300	2.1610	19.1460	0.9610	4.0950	0.0560	5.6380
4931	692.0	0.0350	1.7940	19.0280	0.8840	4.0280	0.0570	5.4170
4934	774.0	0.0320	2.0280	16.9190	1.0380	4.1650	0.0470	5.7270
4937	675.0	0.0350	1.7800	16.9180	0.7630	3.9030	0.0560	5.3320
4941	682.0	0.0270	1.7850	16.0460	0.9550	3.9670	0.0660	5.6210
4955	508.0	0.0260	1.3730	10.9000	0.6150	3.2420	0.0560	4.0630
4964	605.0	0.0260	2.1210	16.2490	0.8830	3.6350	0.0570	4.3760
4970	577.0	0.0310	1.4500	12.6470	0.5280	3.3810	0.0300	5.2000
4980	480.0	0.0280	1.4000	10.7440	0.5000	2.9000	0.0610	2.7600
N	10	10	10	10	10	10	10	10
MEAN	631.9	0.0288	1.7592	15.4486	0.7868	3.7255	0.0531	4.9236
S.D.	94.1	0.0051	0.2876	3.2486	0.1891	0.4215	0.0101	0.9358
S.E.	29.8	0.0016	0.0909	1.0273	0.0598	0.1333	0.0032	0.2959

TABLE 6 (Continued)

ORGAN WEIGHTS
(grams)

52-WEEK SACRIFICE - MALES

GROUP 3 - MEDIUM

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
5079	564.0	0.0290	1.4640	12.6540	0.7310	3.1210	0.0580	5.5320
5080	505.0	0.0330	1.3000	16.0300	0.8950	5.1300	0.0680	4.1000
5090	585.0	0.0340	1.5400	12.3300	0.6770	4.0230	0.0710	4.4550
5093	562.0	0.0310	1.4300	13.4410	0.9200	3.2950	0.0690	4.8920
5096	692.0	0.0240	2.0630	15.8450	0.7470	3.9390	0.0610	5.0640
5099	640.0	0.0380	1.7160	16.1410	0.8390	3.5000	0.0630	5.0750
5102	514.0	0.0360	1.5900	11.6490	0.6500	3.4190	0.0330	3.8710
5114	560.0	0.0380	1.9220	14.0320	0.8220	3.6230	0.0680	4.6440
5120	574.0	0.0280	1.6240	13.1420	0.7180	3.1830	0.0560	2.7710
5139	533.0	0.0290	1.8790	15.0690	1.2040	3.3070	0.0650	4.7350
N	10	10	10	10	10	10	10	10
MEAN	572.9	0.0320	1.6538	14.0312	0.8203	3.6540	0.0612	4.5139
S.D.	56.6	0.0046	0.2404	1.6491	0.1621	0.5992	0.0111	0.7809
S.E.	17.9	0.0015	0.0760	0.5215	0.0513	0.1895	0.0035	0.2469

TABLE 6 (Continued)

ORGAN WEIGHTS
(grams)

52-WEEK SACRIFICE - MALES

GROUP 4 - HIGH

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
5222	685.0	0.0330	1.7350	21.1400	1.1340	4.4850	0.0570	5.7110
5225	647.0	0.0350	1.6100	15.7470	0.7300	3.3330	0.0480	4.9210
5228	474.0	0.0240	1.3320	11.0520	0.6320	2.7860	0.0500	4.4550
5231	551.0	0.0260	1.4250	12.7240	0.6720	3.0240	0.0560	5.0990
5252	585.0	0.0270	1.8420	15.4220	0.8950	3.8810	0.0630	5.0300
5258	558.0	0.0300	1.8310	13.9490	0.7430	4.3700	0.0520	4.6080
5264	464.0	0.0240	1.4150	10.6470	0.6340	2.6470	0.0430	4.5320
5267	666.0	0.0310	1.7050	20.1650	1.0850	3.2120	0.0620	5.4840
5270	609.0	0.0270	1.7300	14.5910	0.8160	3.6450	0.0500	5.1110
5282	530.0	0.0260	1.4350	13.5460	0.6750	3.1440	0.0530	5.6030
N	10	10	10	10	10	10	10	10
MEAN	576.9	0.0285	1.6127	14.8983	0.8016	3.6527	0.0534	5.0554
S.D.	75.2	0.0037	0.1933	3.4659	0.1820	0.8306	0.0062	0.4437
S.E.	24.1	0.0012	0.0611	1.0960	0.0575	0.2627	0.0020	0.1403

TABLE 6 (Continued)

ORGAN WEIGHTS
(grams)

104-WEEK SACRIFICE - MALES

GROUP 1 - CONTROL

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
4522	736.2	0.0120	1.9000	17.8390	0.7960	4.9420	0.2070	6.2210
4523	682.0	0.0190	1.9780	15.7660	0.8600	3.9920	0.0300	7.1090
4525	618.8	0.0580	1.5580	13.9560	0.8040	3.3960	0.0620	5.5000
4526	455.9	0.0220	1.5470	17.0010	0.9620	5.9170	0.0880	5.1870
4527	646.3	0.0310	1.6190	12.2070	0.8400	3.6450	0.0450	2.8580
4529	631.8	0.0100	1.8140	23.5910	1.1040	4.4120	0.0420	4.3350
4530	631.1	0.0200	2.1860	14.2960	0.6940	3.6570	0.0470	5.9180
4531	796.6	0.0260	2.7510	16.8400	1.3740	4.6920	0.0630	6.9350
4533	633.0	0.0460	1.6100	16.7910	0.8780	4.2380	0.0710	5.7390
4535	602.1	0.0330	1.4140	18.1520	2.6120	3.4390	0.0730	4.3950
N	10	10	10	10	10	10	10	10
MEAN	643.4	0.0277	1.8377	16.6439	1.0924	4.2330	0.0728	5.4197
S.D.	89.1	0.0150	0.3974	3.0794	0.5676	0.7922	0.0502	1.2906
S.E.	28.2	0.0047	0.1257	0.9738	0.1795	0.2505	0.0159	0.4081

TABLE 6 (Continued)

ORGAN WEIGHTS
(grams)

104-WEEK SACRIFICE - MALES

GROUP 2 - LOW

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
4573	595.7	0.0320	1.5750	14.4650	0.9310	3.5190	0.0520	4.3910
4575	645.0	0.0380	1.7820	16.3230	0.6270	4.2540	0.0560	5.2830
4576	366.0	0.0370	1.4440	11.4030	0.6940	3.7530	0.1230	2.5930
4578	568.0	0.0370	1.3430	12.7080	0.9420	3.3760	0.0640	4.9380
4579	804.5	0.0440	1.9450	19.6600	1.5890	3.8400	0.0740	6.2670
4582	487.5	0.0260	1.2750	11.2830	0.8410	3.7960	0.0740	5.8870
4583	636.1	0.0340	1.3590	14.8580	0.8500	3.6920	0.0710	5.9930
4584	605.7	0.0280	2.6510	15.1510	0.7540	4.0880	0.0500	5.1920
4587	796.0	0.0470	1.7530	23.4490	1.1010	5.5180	0.0540	5.7440
4588	816.6	0.0410	2.1190	17.5380	1.3900	5.3020	0.1330	6.5560
N	10	10	10	10	10	10	10	10
MEAN	632.1	0.0364	1.7246	15.6838	0.9719	4.1138	0.0751	5.2844
S.D.	144.8	0.0067	0.4280	3.7853	0.3074	0.7292	0.0294	1.1465
S.E.	45.8	0.0021	0.1354	1.1970	0.0972	0.2306	0.0093	0.3625

TABLE 6 (Continued)

ORGAN WEIGHTS
(grams)

104-WEEK SACRIFICE - MALES

GROUP 3 - MEDIUM

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
4623	627.6	0.0310	1.5350	16.9130	0.8520	3.8370	0.0710	5.2430
4625	609.7	0.0350	1.8180	15.7740	1.0510	3.5970	0.0600	4.9570
4626	772.5	0.0460	2.4310	18.9080	1.1690	5.0420	0.0720	6.4430
4627	721.4	0.0490	1.6460	17.8850	0.8390	4.1700	0.0670	6.4810
4630	653.7	0.0550	2.2220	15.9740	1.1380	4.2340	0.1020	5.7430
4632	532.3	0.0430	1.6740	14.8440	0.7480	3.5790	0.0640	5.9290
4633	500.4	0.0640	1.4950	12.5730	0.5760	3.7290	0.1130	3.9510
4634	557.1	0.0290	1.7120	13.1750	0.8470	3.7980	0.0700	5.8190
4635	591.8	0.0360	1.7080	17.3730	0.9630	3.7100	0.1320	5.8120
4636	542.8	0.0450	1.8570	13.5720	0.9620	3.8300	0.0540	4.8960
N	10	10	10	10	10	10	10	10
MEAN	610.9	0.0433	1.8098	15.6941	0.9145	3.9526	0.0805	5.5274
S.D.	86.1	0.0110	0.2978	2.1300	0.1809	0.4397	0.0259	0.7754
S.E.	27.2	0.0035	0.0942	0.6736	0.0572	0.1391	0.0082	0.2452

TABLE 6 (Continued)

ORGAN WEIGHTS
(grams)

104-WEEK SACRIFICE - MALES

GROUP 4 - HIGH

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
4672	678.6	0.0280	2.1350	17.4610	0.9730	4.3650	0.0950	7.0080
4674	720.1	0.0140	1.6320	15.8640	1.0600	4.1350	0.0510	5.6380
4675	754.6	0.0180	1.6860	7.5860	0.7650	4.8700	0.0390	5.7690
4677	605.8	0.0060	1.3550	15.2110	1.1450	4.4100	0.0600	6.4240
4678	600.5	0.0260	1.5870	14.7720	1.0260	3.7430	0.0260	4.5010
4680	712.1	0.0430	1.7040	16.7370	0.7950	3.6890	0.0350	6.3790
4681	468.4	0.0190	1.7710	14.7080	1.5950	3.8710	0.0420	6.2080
4682	561.7	0.0090	2.0880	14.9350	0.7110	3.7440	0.0350	4.2720
4684	584.9	0.0120	1.7060	16.0470	0.9680	4.3890	0.0390	5.6000
4686	555.9	0.0320	1.8770	22.2380	1.4030	5.9820	0.0600	5.2430
N	10	10	10	10	10	10	10	10
MEAN	624.3	0.0207	1.7541	15.5559	1.0441	4.3198	0.0482	5.7042
S.D.	89.6	0.0115	0.2318	3.5803	0.2798	0.6975	0.0198	0.8601
S.E.	28.3	0.0036	0.0733	1.1322	0.0885	0.2206	0.0063	0.2720

TABLE 6 (Continued)

ORGAN WEIGHTS
(grams)

52-WEEK SACRIFICE - FEMALES

GROUP 1 - CONTROL

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
4700	412.0	0.0200	1.1890	9.0620	0.4440	2.1710	0.0730	0.1020
4703	345.0	0.0250	1.2090	9.3260	0.6090	2.4640	0.0850	0.1050
4709	344.0	0.0270	1.2850	7.5250	0.5290	2.0810	0.0710	0.0920
4712	382.0	0.0250	1.1120	10.8100	0.7780	2.5960	0.0920	0.1050
4715	355.0	0.0230	1.1730	9.8880	0.5670	2.2890	0.0810	0.0990
4718	370.0	0.0280	1.2000	9.4140	0.5390	2.1370	0.0890	0.0980
4721	365.0	0.0220	1.0950	9.3810	0.5590	2.1280	0.0730	0.0660
4724	440.0	0.0260	1.3350	11.4000	0.6200	2.3630	0.0820	0.1200
4727	285.0	0.0230	0.9900	6.8200	0.3900	1.8680	0.0640	0.0730
4730	390.0	0.0260	1.1020	8.8420	0.5740	2.1450	0.0710	0.0660
N	10	10	10	10	10	10	10	10
MEAN	368.8	0.0245	1.1670	9.2472	0.5609	2.2242	0.0781	0.0948
S.D.	42.1	0.0025	0.0972	1.3580	0.1041	0.2088	0.0090	0.0159
S.E.	13.3	0.0008	0.0307	0.4294	0.0329	0.0660	0.0029	0.0050

TABLE 6 (Continued)

ORGAN WEIGHTS
(grams)

52-WEEK SACRIFICE - FEMALES

GROUP 2 - LOW

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
4847	308.0	0.0240	1.0970	9.1330	0.4900	1.9580	0.0790	0.0910
4850	365.0	0.0290	1.1850	8.9520	0.5950	2.3850	0.0910	0.0890
4853	311.0	0.0260	1.1130	7.5680	0.5510	2.2780	0.0750	0.0700
4856	335.0	0.0300	1.1230	10.1680	0.4050	2.1750	0.0800	0.0850
4859	405.0	0.0330	1.2350	9.2440	0.5800	2.7080	0.0850	0.1200
4862	268.0	0.0320	0.9420	8.0140	0.3490	2.0090	0.0780	0.1000
4865	429.0	0.0320	1.0400	10.9300	0.5400	2.6060	0.0750	0.1030
4868	482.0	0.0340	1.1580	12.4240	0.6340	2.6360	0.0870	0.0840
4871	399.0	0.0290	1.0400	9.1420	0.4330	2.0520	0.0770	0.1040
4878	310.0	0.0360	1.1590	8.4740	0.7320	2.1720	0.0850	0.1800
N	10	10	10	10	10	10	10	10
MEAN	366.3	0.0305	1.1092	9.4054	0.5409	2.2979	0.0812	0.1026
S.D.	65.6	0.0037	0.0845	1.4362	0.1208	0.2740	0.0055	0.0304
S.E.	20.7	0.0012	0.0267	0.4542	0.0382	0.0867	0.0017	0.0096

TABLE 6 (Continued)

ORGAN WEIGHTS
(grams)

52-WEEK SACRIFICE - FEMALES

GROUP 3 - MEDIUM

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
5003	346.0	0.0290	1.0910	8.8670	0.5230	2.2270	0.0700	0.0980
5006	337.0	0.0290	1.0740	9.0900	0.5110	2.4580	0.0770	0.1080
5015	315.0	0.0330	1.2220	10.4180	0.6610	2.6890	0.0910	0.1120
5018	359.0	0.0310	1.2240	10.3530	0.5560	2.5660	0.0960	0.1530
5022	390.0	0.0360	1.0060	9.5600	0.5270	2.2980	0.0830	0.1500
5025	448.0	0.0400	1.0160	17.2710	0.4310	2.2960	0.1040	0.1940
5039	302.0	0.0310	1.0490	9.0610	0.5300	2.0870	0.0740	0.1080
5054	288.0	0.0280	1.0040	7.7040	0.4220	2.2120	0.0750	0.0990
5060	509.0	0.0300	1.3490	10.7900	0.9780	2.3730	0.0850	0.1240
5067	282.0	0.0270	1.1110	6.8880	0.5150	2.2330	0.0810	0.1070
N	10	10	10	10	10	10	10	10
MEAN	357.6	0.0304	1.1136	10.0222	0.5654	2.3439	0.0836	0.1253
S.D.	73.2	0.0026	0.1155	2.3299	0.1592	0.1814	0.0107	0.0310
S.E.	23.1	0.0008	0.0365	0.8949	0.0503	0.0574	0.0034	0.0098

TABLE 6 (Continued)

ORGAN WEIGHTS
(grams)

52-WEEK SACRIFICE - FEMALES

GROUP 4 - HIGH

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
5150	345.0	0.0250	1.0770	8.6170	0.5280	2.4780	0.0900	0.1600
5153	363.0	0.0230	1.1370	9.6960	0.6110	2.0450	0.0910	0.1660
5156	288.0	0.0190	0.9960	8.3000	0.5560	2.3740	0.0680	0.0890
5159	364.0	0.0250	1.0230	8.9070	0.6630	1.9710	0.0650	0.1030
5162	326.0	0.0250	1.1250	10.2970	0.5120	2.3190	0.0700	0.0810
5165	318.0	0.0250	0.9980	8.9780	0.4630	2.2190	0.0710	0.0890
5168	309.0	0.0200	1.0020	7.4810	0.5320	2.5210	0.0640	0.1010
5171	414.0	0.0370	1.5110	11.5110	0.5900	2.8390	0.0760	0.1600
5174	396.0	0.0250	1.1550	9.5320	0.6060	2.1390	0.0640	0.1500
5177	329.0	0.0280	1.0870	9.0290	0.5950	2.2550	0.0720	0.0650
N	10	10	10	10	10	10	10	10
MEAN	345.2	0.0252	1.1001	9.2250	0.5676	2.3160	0.0731	0.1164
S.D.	39.4	0.0049	0.1655	1.1165	0.0547	0.2543	0.0099	0.0383
S.E.	12.4	0.0016	0.0523	0.3531	0.0173	0.0804	0.0031	0.0121

TABLE 6 (Continued)

ORGAN WEIGHTS
(grams)

104-WEEK SACRIFICE - FEMALES

GROUP 1 - CONTROL

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
4497	292.9	0.0210	0.8860	8.8980	0.5680	2.4510	0.1400	0.1420
4498	366.0	0.0	1.2050	7.8960	0.6510	2.0830	0.0950	0.0
4499	308.3	0.0350	1.4610	12.4510	0.4610	3.3920	0.4790	0.1240
4500	412.1	0.0160	1.1690	9.3890	0.4380	2.0120	0.0410	0.0920
4501	360.3	0.0210	1.3040	9.2000	0.5510	2.6610	0.1190	0.1250
4502	680.4	0.0	1.4340	12.7980	0.8130	2.6960	0.0660	0.0780
4503	486.0	0.0280	1.1250	10.8370	0.3360	2.3200	0.0910	0.1280
4504	363.3	0.0160	0.8510	8.9540	0.3120	2.3660	0.0540	0.0880
4505	388.8	0.0060	1.0070	8.9270	0.3700	2.1960	0.0600	0.0760
4508	526.8	0.0570	1.3360	14.4950	0.4710	3.4130	0.0770	0.0920
N	10	8	10	10	10	10	10	9
MEAN	418.5	0.0250	1.1779	10.3845	0.4971	2.5590	0.1222	0.9939
S.D.	116.9	0.0155	0.2138	2.1644	0.1539	0.4962	0.1290	2.6559
S.E.	37.0	0.0055	0.0676	0.6845	0.0487	0.1569	0.0408	0.8853

TABLE 6 (Continued)

ORGAN WEIGHTS
(grams)

104-WEEK SACRIFICE - FEMALES

GROUP 2 - LOW

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
4548	367.1	0.0260	1.0150	10.3230	0.6160	3.0650	0.1330	0.0600
4549	426.2	0.0400	1.4270	12.4720	0.5660	3.5160	0.0750	0.0490
4550	419.0	0.0340	1.5820	11.7310	0.5850	2.9470	0.0620	0.0730
4551	406.0	0.0560	1.6270	14.2900	0.8780	3.8850	0.2830	0.1280
4552	349.9	0.0370	1.0340	12.6430	0.7920	3.5790	0.1280	0.0280
4553	426.1	0.0340	1.1580	10.9570	0.5440	2.6200	0.0890	0.0640
4554	313.9	0.0290	1.4600	9.4000	0.6010	2.7400	0.0980	0.0500
4556	308.0	0.0310	1.4930	9.2720	0.6910	2.3820	0.1470	0.0560
4557	338.8	0.0420	1.4090	10.6210	2.0990	1.8790	0.0940	0.0500
4558	344.0	0.0600	1.0540	9.3300	0.5040	2.6870	0.1440	0.0550
N	10	10	10	10	10	10	10	10
MEAN	369.9	0.0389	1.3259	11.1039	0.7876	2.9300	0.1253	0.1213
S.D.	46.0	0.0112	0.2365	1.6685	0.4751	0.6047	0.0627	0.1911
S.E.	14.6	0.0035	0.0748	0.5276	0.1502	0.1912	0.0198	0.0604

TABLE 6 (Continued)

ORGAN WEIGHTS
(grams)

104-WEEK SACRIFICE - FEMALES

GROUP 3 - MEDIUM

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
4598	450.0	0.0370	1.0410	9.9920	0.6540	2.5660	0.0810	0.0440
4599	371.2	0.0300	1.2280	9.5070	0.5150	2.5960	0.0690	0.0800
4600	346.5	0.0350	0.9530	9.7560	0.7090	2.6620	0.1930	0.0590
4602	294.8	0.0230	1.3000	7.4280	0.4210	2.2970	0.0600	0.0340
4603	348.8	0.0310	1.0170	8.5790	0.3530	2.0580	0.1200	0.0500
4605	320.0	0.0340	1.0920	8.8990	0.4270	2.4900	0.0850	0.0620
4606	406.2	0.0370	1.3250	9.7260	0.5270	2.3250	0.0630	0.1060
4609	339.2	0.0380	0.7250	7.1820	0.4830	2.0940	0.4630	0.0880
4611	464.5	0.0300	2.0940	12.0610	0.6920	3.4730	1.2570	0.0670
4612	331.3	0.0280	1.3530	9.0970	0.6110	1.9210	0.0860	0.0650
N	10	10	10	10	10	10	10	10
MEAN	367.2	0.0323	1.2128	9.2227	0.5392	2.4482	0.2477	0.0655
S.D.	55.9	0.0048	0.3658	1.3819	0.1228	0.4381	0.3751	0.0214
S.E.	17.7	0.0015	0.1157	0.4370	0.0388	0.1385	0.1186	0.0068

TABLE 6 (Continued)

ORGAN WEIGHTS
(grams)

104-WEEK SACRIFICE - FEMALES

GROUP 4 - HIGH

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
4647	328.1	0.0070	1.2600	8.2630	0.5330	1.9590	0.0520	0.0880
4648	398.4	0.0150	1.4140	11.0770	0.5820	2.6220	0.0670	0.1090
4650	369.1	0.0120	0.9390	8.5610	0.5160	2.1900	0.0660	0.1120
4651	302.4	0.0230	1.0400	8.9150	0.5160	2.3550	0.1080	0.1280
4652	321.8	0.0350	1.3290	10.9720	1.8360	2.9070	0.3470	0.1000
4653	502.5	0.0100	1.9710	13.9740	0.8560	3.2680	0.0620	0.0
4654	404.3	0.0180	1.4950	9.4450	0.3370	2.2460	0.0	0.1370
4655	360.2	0.0160	1.0040	8.0620	0.4210	2.0470	0.0530	0.0930
4657	348.6	0.0280	1.5770	16.0360	0.7790	5.8100	0.1260	0.1200
4658	297.2	0.0350	1.4560	9.1170	0.4270	2.1850	0.0780	0.1300
N	10	10	10	10	10	10	9	9
MEAN	363.3	0.0199	1.3485	10.4422	0.6803	2.7589	0.1066	0.1130
S.D.	61.1	0.0100	0.3103	2.6559	0.4360	1.1467	0.0936	0.0171
S.E.	19.3	0.0032	0.0981	0.8399	0.1379	0.3626	0.0312	0.0057

TABLE 7

ORGAN WEIGHT-BODY WEIGHT PERCENTAGES

52-WEEK SACRIFICE - MALES

GROUP 1 - CONTROL

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
4772	0.0035	0.2131	2.2432	0.1094	0.6225	0.0078	0.8526
4775	0.0036	0.2521	2.2112	0.1319	0.5681	0.0104	0.9009
4781	0.0049	0.3023	2.4592	0.1274	0.6645	0.0096	0.7352
4784	0.0038	0.2525	1.9874	0.1647	0.5015	0.0086	0.8777
4787	0.0045	0.2483	2.1531	0.1219	0.5124	0.0081	1.0080
4790	0.0045	0.2544	2.2477	0.1456	0.5603	0.0115	0.7988
4793	0.0049	0.2595	2.4079	0.1322	0.6918	0.0082	0.8543
4796	0.0050	0.2752	2.7392	0.1809	0.5890	0.0107	0.8690
4799	0.0046	0.2456	2.7201	0.1107	0.7100	0.0098	0.7511
4802	0.0049	0.2835	2.7058	0.1687	0.6621	0.0098	0.9415
N	10	10	10	10	10	10	10
MEAN	0.0044	0.2636	2.3941	0.1398	0.6082	0.0095	0.8589
S.D.	0.0006	0.0262	0.2525	0.0254	0.0734	0.0012	0.0829
S.E.	0.0002	0.0083	0.0830	0.0080	0.0232	0.0004	0.0262

TABLE 7 (Continued)

ORGAN WEIGHT-BODY WEIGHT PERCENTAGES

52-WEEK SACRIFICE - MALES

GROUP 2 - LOW

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
4922	0.0030	0.2824	2.3005	0.1231	0.6543	0.0075	0.8475
4928	0.0041	0.2985	2.6445	0.1327	0.5656	0.0077	0.7787
4931	0.0051	0.2592	2.7491	0.1277	0.5421	0.0082	0.7828
4934	0.0041	0.2620	2.4443	0.1341	0.5381	0.0061	0.7399
4937	0.0052	0.2637	2.5064	0.1130	0.5762	0.0083	0.7849
4941	0.0040	0.2617	2.3528	0.1400	0.5817	0.0097	0.8242
4955	0.0051	0.2703	2.1457	0.1211	0.6382	0.0110	0.7998
4964	0.0043	0.3506	2.6924	0.1460	0.6008	0.0094	0.7233
4970	0.0054	0.2513	2.1919	0.0915	0.5860	0.0052	0.9012
4980	0.0058	0.2917	2.2383	0.1042	0.6042	0.0127	0.5750
N	10	10	10	10	10	10	10
MEAN	0.0046	0.2791	2.4206	0.1233	0.5929	0.0086	0.7762
S.D.	0.0008	0.0293	0.2160	0.0167	0.0338	0.0022	0.0872
S.E.	0.0003	0.0093	0.0683	0.0053	0.0107	0.0007	0.0276

TABLE 7 (Continued)

ORGAN WEIGHT-BODY WEIGHT PERCENTAGES

52-WEEK SACRIFICE - MALES

GROUP 3 - MEDIUM

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
5079	0.0051	0.2603	2.2399	0.1296	0.5534	0.0103	0.9809
5080	0.0065	0.2574	2.1743	0.1772	1.0158	0.0135	0.8119
5090	0.0058	0.2643	2.1077	0.1157	0.6877	0.0121	0.7615
5093	0.0055	0.2544	2.3916	0.1637	0.5863	0.0123	0.8705
5095	0.0035	0.2981	2.2897	0.1079	0.5692	0.0088	0.7318
5099	0.0059	0.2681	2.5220	0.1311	0.5469	0.0098	0.7930
5102	0.0070	0.3093	2.2663	0.1265	0.6652	0.0064	0.7531
5114	0.0068	0.3432	2.5057	0.1468	0.6470	0.0121	0.8293
5120	0.0049	0.2829	2.2895	0.1251	0.5545	0.0098	0.4828
5139	0.0054	0.3525	2.8272	0.2259	0.6205	0.0122	0.8884
N	10	10	10	10	10	10	10
MEAN	0.0057	0.2891	2.4014	0.1450	0.6446	0.0107	0.7903
S.D.	0.0010	0.0359	0.3204	0.0355	0.1397	0.0021	0.1310
S.E.	0.0003	0.0113	0.1013	0.0112	0.0442	0.0007	0.0414

TABLE 7 (Continued)

ORGAN WEIGHT-BODY WEIGHT PERCENTAGES

52-WEEK SACRIFICE - MALES

GROUP 4 - HIGH

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
5222	0.0048	0.2533	3.0461	0.1655	0.6547	0.0083	0.8337
5225	0.0054	0.2488	2.4338	0.1128	0.5151	0.0074	0.7606
5228	0.0051	0.2810	2.3316	0.1333	0.5878	0.0105	0.9399
5231	0.0047	0.2593	2.3093	0.1220	0.5488	0.0102	0.9254
5252	0.0045	0.3149	2.6362	0.1530	0.6634	0.0108	0.8598
5258	0.0054	0.3281	2.4998	0.1332	0.7832	0.0093	0.8258
5264	0.0052	0.3050	2.2946	0.1366	0.5705	0.0093	0.9767
5267	0.0047	0.2655	3.0278	0.1629	0.7826	0.0093	0.8234
5270	0.0044	0.2841	2.3959	0.1340	0.5985	0.0082	0.8392
5282	0.0053	0.2708	2.5558	0.1274	0.5932	0.0100	1.0572
N	10	10	10	10	10	10	10
MEAN	0.0050	0.2811	2.5571	0.1381	0.6298	0.0093	0.8842
S.D.	0.0004	0.0270	0.2854	0.0172	0.0918	0.0011	0.0887
S.E.	0.0001	0.0085	0.0903	0.0054	0.0290	0.0003	0.0281

TABLE 7 (Continued)

ORGAN WEIGHT-BODY WEIGHT PERCENTAGES

104-WEEK SACRIFICE - MALES

GROUP 1 - CONTROL

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRE'LS	TESTES
4522	0.0016	0.2581	2.4231	0.1081	0.6713	0.0281	0.8450
4523	0.0028	0.2900	2.3117	0.1261	0.5853	0.0044	1.0424
4525	0.0094	0.2518	2.2553	0.1299	0.5488	0.0100	0.8888
4526	0.0048	0.3393	3.7291	0.2110	1.2979	0.0193	1.1377
4527	0.0048	0.2505	1.8888	0.1300	0.5640	0.0070	0.4422
4529	0.0016	0.2871	3.7339	0.1747	0.6983	0.0066	0.6861
4530	0.0032	0.3464	2.2653	0.1100	0.5795	0.0074	0.9377
4531	0.0033	0.3453	2.1140	0.1725	0.5890	0.0079	0.8706
4533	0.0073	0.2543	2.6526	0.1387	0.6695	0.0112	0.9066
4535	0.0055	0.2348	3.0148	0.4338	0.5712	0.0121	0.7299
N	10	10	10	10	10	10	10
MEAN	0.0044	0.2858	2.6389	0.1735	0.6775	0.0114	0.8487
S.D.	0.0025	0.0433	0.6504	0.0970	0.2241	0.0072	0.1944
S.E.	0.0008	0.0137	0.2057	0.0307	0.0709	0.0023	0.0615

TABLE 7 (Continued)

ORGAN WEIGHT-BODY WEIGHT PERCENTAGES

104-WEEK SACRIFICE - MALES

GROUP 2 - LOW

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
4573	0.0054	0.2644	2.4282	0.1563	0.5907	0.0087	0.7371
4575	0.0059	0.2763	2.5307	0.0972	0.6595	0.0087	0.8191
4576	0.0101	0.3945	3.1156	0.1896	1.0254	0.0336	0.7065
4578	0.0065	0.2364	2.2373	0.1658	0.5944	0.0113	0.8694
4579	0.0055	0.2418	2.4438	0.1975	0.4773	0.0092	0.7790
4582	0.0053	0.2615	2.3145	0.1725	0.7787	0.0152	1.2076
4583	0.0053	0.2136	2.3358	0.1336	0.5804	0.0112	0.9421
4584	0.0046	0.4377	2.5014	0.1245	0.6749	0.0083	0.8572
4587	0.0059	0.2202	2.9459	0.1383	0.6932	0.0068	0.7216
4588	0.0050	0.2595	2.1477	0.1702	0.6493	0.0163	0.8028
N	10	10	10	10	10	10	10
MEAN	0.0060	0.2806	2.5001	0.1546	0.6724	0.0129	0.8444
S.D.	0.0015	0.0748	0.3058	0.0310	0.1477	0.0079	0.1468
S.E.	0.0005	0.0236	0.0967	0.0098	0.0467	0.0025	0.0464

TABLE 7 (Continued)

ORGAN WEIGHT-BODY WEIGHT PERCENTAGES

104-WEEK SACRIFICE - MALES

GROUP 3 - MEDIUM

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
4623	0.0049	0.2446	2.6949	0.1358	0.6114	0.0113	0.8354
4625	0.0057	0.2982	2.5872	0.1724	0.5900	0.0098	0.8130
4626	0.0060	0.3147	2.4476	0.1513	0.6527	0.0093	0.8340
4627	0.0068	0.2282	2.4792	0.1163	0.5780	0.0093	0.8984
4630	0.0084	0.3399	2.4436	0.1741	0.6477	0.0156	0.8785
4632	0.0081	0.3145	2.7887	0.1405	0.6724	0.0120	1.1138
4633	0.0128	0.2988	2.5126	0.1151	0.7452	0.0226	0.7896
4634	0.0052	0.3073	2.3649	0.1520	0.6817	0.0126	1.0445
4635	0.0061	0.2886	2.9356	0.1627	0.6269	0.0223	0.9621
4636	0.0083	0.3421	2.5004	0.1772	0.7056	0.0099	0.9020
N	10	10	10	10	10	10	10
MEAN	0.0072	0.2977	2.5755	0.1497	0.6512	0.0135	0.9091
S.D.	0.0023	0.0368	0.1784	0.0227	0.0521	0.0051	0.1061
S.E.	0.0007	0.0116	0.0564	0.0072	0.0165	0.0016	0.0335

TABLE 7 (Continued)

ORGAN WEIGHT-BODY WEIGHT PERCENTAGES

104-WEEK SACRIFICE - MALES

GROUP 4 - HIGH

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
4672	0.0041	0.3146	2.5731	0.1434	0.6432	0.0140	1.0327
4674	0.0019	0.2266	2.2030	0.1472	0.5742	0.0071	0.7829
4675	0.0024	0.2234	1.0053	0.1014	0.6454	0.0052	0.7645
4677	0.0010	0.2237	2.5109	0.1890	0.7280	0.0099	1.0604
4678	0.0043	0.2643	2.4599	0.1709	0.6233	0.0043	0.7495
4680	0.0060	0.2393	2.3504	0.1116	0.5180	0.0049	0.8958
4681	0.0041	0.3781	3.1401	0.3405	0.8264	0.0090	1.3254
4682	0.0016	0.3717	2.6589	0.1266	0.6665	0.0062	0.7605
4684	0.0021	0.2917	2.7435	0.1655	0.7504	0.0067	0.9574
4686	0.0058	0.3377	4.0004	0.2524	1.0761	0.0108	0.9432
N	10	10	10	10	10	10	10
MEAN	0.0033	0.2871	2.5645	0.1748	0.7052	0.0078	0.9272
S.D.	0.0018	0.0608	0.7495	0.0724	0.1573	0.0031	0.1814
S.E.	0.0006	0.0192	0.2370	0.0229	0.0497	0.0010	0.0574

TABLE 7 (Continued)

ORGAN WEIGHT-BODY WEIGHT PERCENTAGES

52-WEEK SACRIFICE - FEMALES

GROUP 1 - CONTROL

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
4700	0.0045	0.2486	2.1995	0.1074	0.5269	0.0177	0.0248
4703	0.0072	0.3504	2.7032	0.1765	0.7142	0.0246	0.0304
4709	0.0078	0.3677	2.1475	0.1510	0.6049	0.0206	0.0267
4712	0.0065	0.2911	2.8298	0.2037	0.6796	0.0241	0.0275
4715	0.0065	0.3304	2.7454	0.1591	0.6448	0.0228	0.0279
4718	0.0076	0.3243	2.5434	0.1457	0.5776	0.0241	0.0265
4721	0.0060	0.3000	2.5701	0.1532	0.5830	0.0200	0.0241
4724	0.0059	0.3034	2.5409	0.1409	0.5370	0.0186	0.0213
4727	0.0081	0.3474	2.3430	0.1364	0.6554	0.0225	0.0256
4730	0.0067	0.2826	2.2572	0.1472	0.5500	0.0182	0.0169
N	10	10	10	10	10	10	10
MEAN	0.0067	0.3186	2.5072	0.1525	0.6074	0.0213	0.0258
S.D.	0.0010	0.0297	0.2351	0.0252	0.0637	0.0026	0.0036
S.E.	0.0003	0.0094	0.0745	0.0080	0.0201	0.0008	0.0011

TABLE 7 (Continued)

ORGAN WEIGHT-BODY WEIGHT PERCENTAGES

52-WEEK SACRIFICE - FEMALES

GROUP 2 - LOW

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
4847	0.0078	0.3562	2.9053	0.1591	0.6357	0.0256	0.0295
4850	0.0079	0.3247	2.4526	0.1630	0.6534	0.0249	0.0244
4853	0.0084	0.3579	2.4334	0.2093	0.7325	0.0241	0.0225
4856	0.0090	0.3352	3.0352	0.1209	0.6493	0.0239	0.0254
4859	0.0081	0.3049	2.2825	0.1432	0.6686	0.0210	0.0296
4862	0.0119	0.3515	2.9903	0.1302	0.7496	0.0291	0.0373
4865	0.0076	0.2476	2.5024	0.1286	0.6205	0.0179	0.0245
4868	0.0071	0.2402	2.5246	0.1315	0.5469	0.0180	0.0174
4871	0.0073	0.2607	2.2912	0.1085	0.5143	0.0193	0.0261
4898	0.0116	0.3734	2.7152	0.2361	0.7006	0.0274	0.0581
N	10	10	10	10	10	10	10
MEAN	0.0087	0.3153	2.6356	0.1531	0.6471	0.0231	0.0295
S.D.	0.0017	0.0495	0.2841	0.0407	0.0743	0.0039	0.0113
S.E.	0.0005	0.0156	0.0898	0.0129	0.0235	0.0012	0.0036

TABLE 7 (Continued)

ORGAN WEIGHT-BODY WEIGHT PERCENTAGES

52-WEEK SACRIFICE - FEMALES

GROUP 3 - MEDIUM

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
5003	0.0084	0.3153	2.5027	0.1512	0.6436	0.0202	0.0283
5006	0.0086	0.3187	2.6773	0.1516	0.7294	0.0228	0.0320
5015	0.0105	0.3879	3.3073	0.2698	0.8537	0.0289	0.0356
5018	0.0086	0.3409	2.9396	0.1549	0.7148	0.0267	0.0426
5022	0.0092	0.2579	2.4514	0.1351	0.5892	0.0213	0.0385
5025	0.0067	0.2268	3.4551	0.0962	0.5125	0.0232	0.0433
5039	0.0103	0.3440	3.0070	0.1755	0.6911	0.0245	0.0358
5054	0.0097	0.3486	2.6750	0.1465	0.7681	0.0260	0.0344
5060	0.0059	0.2650	2.1198	0.1921	0.4662	0.0167	0.0244
5067	0.0096	0.3940	2.4426	0.1826	0.7918	0.0287	0.0379
N	10	10	10	10	10	10	10
MEAN	0.0087	0.3199	2.8058	0.1596	0.6760	0.0239	0.0353
S.D.	0.0015	0.0553	0.4974	0.0322	0.1235	0.0039	0.0059
S.E.	0.0005	0.0175	0.1573	0.0102	0.0391	0.0012	0.0019

TABLE 7 (Continued

ORGAN WEIGHT-BODY WEIGHT PERCENTAGES

52-WEEK SACRIFICE - FEMALES

GROUP 4 - HIGH

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
5150	0.0072	0.3122	2.4977	0.1530	0.7183	0.0261	0.0464
5153	0.0063	0.3132	2.6716	0.1683	0.5634	0.0251	0.0457
5156	0.0066	0.3076	2.8819	0.1931	0.8243	0.0236	0.0309
5159	0.0069	0.2810	2.4470	0.1821	0.5415	0.0179	0.0283
5162	0.0077	0.3451	3.1586	0.1571	0.7113	0.0215	0.0248
5165	0.0079	0.3138	2.7918	0.1519	0.6978	0.0223	0.0280
5168	0.0065	0.3243	2.4210	0.1722	0.8159	0.0207	0.0327
5171	0.0089	0.3650	2.7804	0.1425	0.6857	0.0184	0.0386
5174	0.0063	0.2917	2.4071	0.1530	0.5402	0.0162	0.0379
5177	0.0095	0.3304	2.7444	0.1809	0.6854	0.0219	0.0199
N	10	10	10	10	10	10	10
MEAN	0.0073	0.3184	2.6402	0.1654	0.6784	0.0214	0.0333
S.D.	0.0009	0.0244	0.2417	0.0164	0.1024	0.0032	0.0068
S.E.	0.0003	0.0077	0.0764	0.0052	0.0324	0.0010	0.0028

TABLE 7 (Continued)

ORGAN WEIGHT-BODY WEIGHT PERCENTAGES

104-WEEK SACRIFICE - FEMALES

GROUP 1 - CONTROL

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
4497	0.0072	0.3025	3.0379	0.1939	0.8368	0.0478	0.0485
4498	0.0	0.3295	2.1574	0.1779	0.5691	0.0260	0.0
4499	0.0114	0.4739	4.0386	0.1495	1.1002	0.1554	0.0402
4500	0.0039	0.2837	2.2783	0.1063	0.4882	0.0099	0.0223
4501	0.0058	0.3619	2.5534	0.1529	0.7386	0.0330	0.0347
4502	0.0	0.2108	1.8810	0.1195	0.3962	0.0097	0.0115
4503	0.0058	0.2315	2.2298	0.0691	0.4774	0.0187	0.0263
4504	0.0044	0.2342	2.4646	0.0859	0.6513	0.0149	0.0242
4505	0.0015	0.2590	2.2960	0.0952	0.5648	0.0154	2.0772
4508	0.0108	0.2536	2.7515	0.0894	0.6479	0.0146	0.0175
N	8	10	10	10	10	10	9
MEAN	0.0063	0.2941	2.5689	0.1240	0.6470	0.0345	0.2558
S.D.	0.0034	0.0787	0.6093	0.0423	0.2054	0.0441	0.6831
S.E.	0.0012	0.0249	0.1927	0.0134	0.0649	0.0139	0.2277

TABLE 7 (Continued)

ORGAN WEIGHT-BODY WEIGHT PERCENTAGES

104-WEEK SACRIFICE - FEMALES

GROUP 2 - LOW

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
4548	0.0071	0.2765	2.8120	0.1678	0.8349	0.0362	0.1798
4549	0.0094	0.3348	2.9263	0.1328	0.8250	0.0176	0.0115
4550	0.0081	0.3776	2.7998	0.1396	0.7033	0.0148	0.0174
4551	0.0138	0.4007	3.5197	0.2163	0.9569	0.0697	0.0315
4552	0.0106	0.2955	3.6133	0.2264	1.0229	0.0366	0.0080
4553	0.0080	0.2718	2.5715	0.1277	0.6149	0.0209	0.0150
4554	0.0092	0.4651	2.9946	0.1915	0.8729	0.0312	0.0159
4556	0.0101	0.4847	3.0104	0.2244	0.7734	0.0477	0.0182
4557	0.0124	0.4159	3.1349	0.6195	0.5546	0.0277	0.0148
4558	0.0174	0.3064	2.7122	0.1465	0.7811	0.0419	0.0160
N	10	10	10	10	10	10	10
MEAN	0.0106	0.3629	3.0095	0.2192	0.7940	0.0344	0.0328
S.D.	0.0031	0.0775	0.3352	0.1458	0.1437	0.0163	0.0520
S.E.	0.0010	0.0245	0.1060	0.0461	0.0455	0.0052	0.0164

TABLE 7 (Continued)

ORGAN WEIGHT-BODY WEIGHT PERCENTAGES

104-WEEK SACRIFICE - FEMALES

GROUP 3 - MEDIUM

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
4598	0.0062	0.2313	2.2204	0.1453	0.5702	0.0180	0.0098
4599	0.0081	0.3308	2.5612	0.1387	0.6994	0.0186	0.0216
4600	0.0101	0.2750	2.8156	0.2046	0.7683	0.0557	0.0170
4602	0.0078	0.4410	2.5197	0.1428	0.7792	0.0204	0.0115
4603	0.0089	0.2916	2.4596	0.1012	0.5900	0.0344	0.0143
4605	0.0106	0.3413	2.7809	0.1334	0.7781	0.0266	0.0194
4606	0.0091	0.3262	2.3944	0.1297	0.5724	0.0155	0.0261
4609	0.0112	0.2137	2.1173	0.1424	0.6173	0.1365	0.0259
4611	0.0065	0.4508	2.5966	0.1490	0.7477	0.2706	0.0144
4612	0.0085	0.4084	2.7458	0.1844	0.5798	0.0260	0.0196
N	10	10	10	10	10	10	10
MEAN	0.0089	0.3310	2.5211	0.1472	0.6702	0.0622	0.0180
S.D.	0.0014	0.0823	0.2322	0.0287	0.0925	0.0817	0.0056
S.E.	0.0005	0.0260	0.0734	0.0091	0.0292	0.0259	0.0018

TABLE 7 (Continued)

ORGAN WEIGHT-BODY WEIGHT PERCENTAGES

104-WEEK SACRIFICE - FEMALES

GROUP 4 - HIGH

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
4647	0.0021	0.3840	2.5184	0.1625	0.5971	0.0158	0.0268
4648	0.0038	0.3549	2.7804	0.1461	0.6581	0.0168	0.0274
4650	0.0033	0.2544	2.3194	0.1398	0.5933	0.0179	0.0303
4651	0.0076	0.3439	2.9481	0.1706	0.7788	0.0357	0.0423
4652	0.0109	0.4130	3.4096	0.5705	0.9034	0.1078	0.0311
4653	0.0020	0.3922	2.7809	0.1703	0.6503	0.0123	0.0
4654	0.0045	0.3698	2.3361	0.0834	0.5555	0.0	0.0339
4655	0.0044	0.2787	2.2382	0.1169	0.5683	0.0147	0.0258
4657	0.0080	0.4524	4.6001	0.2235	1.6667	0.0361	0.0344
4658	0.0118	0.4899	3.0676	0.1437	0.7352	0.0262	0.0437
N	10	10	10	10	10	9	9
MEAN	0.0058	0.3733	2.8999	0.1927	0.7707	0.0315	0.0329
S.D.	0.0035	0.0716	0.7030	0.1377	0.3330	0.0300	0.0065
S.E.	0.0011	0.0227	0.2223	0.0435	0.1053	0.0100	0.0022

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUND

Group 1 - Males

Animal #	Gross Findings: Tissue Masses	Gross Findings: Other
4524		NGL
4528		Pit.-enlarged; lf. lung-dark red; thick stomach walls.
4532	Rt. kid., adrenal involved in mass.	Lungs-white spots; lf. kidney-pale; bloody fluid in scrotal sacs; red fluid in abd. cavity.
4534		NGL
4536		Lung-mottled; renal pelvis dilated; lf. kidney-red fluid, blister-like area; mes. lymph node, enlarged, dark; bladder-red fluid, distended.
4541		Brain-soft, red clot on surface; kidney-pelvis dilated.
4774		Lungs-dark red; mes. arteries-hard, tortuous.
4776		Testes, sem. ves.-atrophied; kidney-enlarged, pitted; pelvis-dilated; lungs-mottled.
4778*		Hind quarters-paralized; pit.-greatly enlarged, black.
4779		Brain-adhered to skull; soft, clear fluid around brain; skull-indented, rt. side; ribs,sternum-misshaped.
4780		Kidney, liver-enlarged; liver-nottled; lungs-lg. red spots; int.-dark red.
4783*		Eyes, nostrils-bloody crust; GI tract-gray mucous.
4786		Lungs-hem.; kidneys-pelvis dilated, contains red fluid; stomach-pylorus blocked by hair ball; bladder-thick blood-colored fluid with clot; sem. ves . dark red.
4791	Sm. t.m.-mesentery.	Pit.-enlarged; lungs-hem.,mottled; thymus-enlarged; thoracic cavity-red fluid; liver, kidney, adrenal-enlarged; abd. cavity-red, watery fluid; testes, sem. ves.-atrophied.
4795	Lg. intestine-firm t.m.	Badly cannibalized.
4797		Rt. testicle-atrophied; nostrils, lungs-frothy discharge; liver-gran. appearance.

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUND

Group 1 - Males (contd)

Animal #	Gross Findings: Tissue Masses	Gross Findings: Other
4798		GI tract-red mucous; lungs-bright in color.
4803		Pit.-enlarged, lt. color; lungs-lf. lobe dark spots; kidneys-pale; GI tract-yellow mucous.
4808	Sm.nodular mass-rt. pelvic region.	Lungs-dark red; liver-pale, kid.-enlarged.
4815		Thyrds-enlarged; lungs-dark red; liver-dark, enlarged; kidneys-mottled, enlarged; GI tract-red mucous; testes, sem. ves.-atrophied
4818		Pit.-enlarged, black; lungs-dark red, splotchy; rt. kidney-blister; stomach-impacted with food, hair; testes-small; mammary tissue-active.
4819		Pit.-greatly enlarged.
4820*	Mass attached rt. ear (70gm).	Spleen-greatly enlarged.
4823		Pit.-greatly enlarged; lungs-red fluid; kidneys-pale; testes, sem. ves.-atrophied; thoracic, abd. cavity-red fluid.
4824*		Pit.-greatly enlarged.
4825		Pit.-enlarged, pale; lungs-congested; thymus, liver, kidneys, spleen-extrem. lg.; renal pelvis-gone; stomach walls-thickened; GI tract-empty, hem., testes, sem. ves.-atrophied; lymph nodes-greatly enlarged; salv. glands-greatly enlarged; all tissues, organs have greenish-yellow slim appearance.
4826*	Mass-rt. adrenal-adhered to liver/kidney.	Pit.-greatly enlarged; lungs-nodules; lf. adrenal-sm., testes, sem. ves.-small; paralysis.
4827	Lf. eye- sm. mass or abscess.	Stomach-walls thickened. mes. lymph nodes-enlarged.
4829	White mass along optic nerve.	Supra-orbital lymph node-abscessed leading into skull under brain involving pit.; thick white pus under brain; Abscess-lung, lf. lobe-lung adhered to chest wall; abscess-rt. ventral pelvis; testes, sem. ves.-atrophied.

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUND

Group 1 - Males (contd)

Animal #	Gross Findings: Tissue Masses	Gross Findings: Other
4832	Lg. t.m.-thoracic, lf. ventral (624gm).	Spleen-enlarged, round margins; stomach-impacted with hair,food, bedding; bladder-red fluid; rt. sem. ves.-atrophied.
4836		Cannibalized.
4841	Hard mass-lumbar region.	Lungs-hem.; pelvis-dilated; one adrenal-enlarged.
4843		Lungs, liver-pale; kidneys, adrenals-enlarged, gray.
4845		Died 2/2/75 Necropsy Sheet missing

*sacrificed-moribund

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUND

Group 2 - Males

Animal #	Gross Findings: Tissue Masses	Gross Findings: Other
4572	T.M.-rt. thoracic ventral (239gm).	Lungs-mottled; heart-enlarged; liver-enlarged, mottled, pale; spleen-enlarged, rounded margins; kidneys-enlarged, contain pus; pelvis-dilated; adrenals-enlarged; bladder-thick walls; sem. ves.-atrophied.
4574		Lungs-mottled.
4577*	T.M. or swelling-rt. side head.	Liver-pale; spleen-slightly enlarged.
4580		Spleen-small.
4581		Lf. hind foot-abscess.
4585		Brain-red fluid, lf. side; cervical lymphs-bright red,enlarged; lungs-hem., light areas; stomach walls-appear thick; mes.-dark, prominent; kidneys-pelvis dilated; liver-pinpoint yellow spots all lobes.
4586	Pancreas possibly involved in mass surrounding spleen.	Unclotted blood over brain; rt. lung-white nodules, adhered to diaphragm; pancreas-thickened; yellow, cloudy fluid-abd. cavity; spleen, cecum, stomach-adhered.
4591		Lung-bright red; kidneys-pale, blistered; dorsal aorta-thickened walls; prostate-abscessed.
4924		Lungs-hem.; spleen-slightly enlarged; kidneys-pitted.
4930	Lg. t.m.-head/neck.	Autolyzed.
4933	Med. size t.m.-abd. cavity, adhered to GI tract, testicular fat.	Lungs-dark red; spleen-enlarged.
4939		Pit.-greatly enlarged; lungs-mottled.
4942		Autolysis.
4943		Clear watery fluid in chest cavity; lungs-bright red; kidneys-pitted, pale, pelvis dilated; testes-atrophied.
4948		Lungs-white areas; liver-enlarged; kidneys-white area-pelvis; dark red fluid in scrotum.

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUND

Group 2 - Males (contd)

Animal #	Gross Findings: Tissue Masses	Gross Findings: Other
4954		Thyroid-bright red; lungs-mottled, red fluid; Pyers' patches prom.; mes. lymph-dark; sal., cervical lymphs-enlarged, dark.
4956	Med. t.m.-rt. abd., ventral (60gm)	Pit.-greatly enlarged; lungs-splotchy.
4959	Sm. t.m.-head, neck, ventral (19gm).	Lungs, liver-pale; heart, spleen-enlarged; rt. ear thickened, ulcerated.
4960		Lungs-mottled; liver-mottled.
4962		NGL
4963		Rt. eye-protruding; liver, spleen, kidney-enlarged; kidney-pale; liver-rounded margins; mes. lymph node-enlarged.
4971	T.M.-lf. thoracic (38gm).	Pit.-enlarged, dark red; scrotal hernia; hermaphroditic, uterus, ovaries, penis; no testes; sem. ves.-small.
4972		Lung-congested; heart-rt. auricle dilated; kidneys-greatly enlarged, pelvis dilated, red; urine in bladder.
4975	T.M.-lf. pelvic ventral, med.(111gm).	Paralysis-hind quarters before death; kidneys-pitted; arenals-speckled.
4982	Med. mass-mesentery (93gm); mass attached to lwr. rt. lobe-lung.	Lungs-bright colored; blood colored urine in bladder.
4984	Nodule on thoracic spinal column.	Red material on brain surface; thyroid-slightly enlarged; lung-rt. lobe dark red; liver-greatly enlarged, lobes thick, margins rounded; spleen-enlarged; kidneys-cortex wide, pitted, wide striated zone between cortex, medulla; cervical lymphs-dark red; free fluid-red in abd. cavity; adrenals-slightly enlarged.
4987		Pit.-greatly enlarged, dark; blood colored fluid in chest cavity; kidney-pelvis dilated.

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUND

Group 2 - Males (contd)

Animal #	Gross Findings: Tissue Masses	Gross Findings: Other
4989		Lungs-congested; white object in bladder neck.
4994	T.M.-ulcerated, lf. axilla, small, (18gm).	Testes-pale; spleen-slightly thickened; liver-very pale, margins rounded; kidney-wide striated zone between medulla, cortex; brain, pit., thyroid-pale.
4995		Lung-hem.

*sacrificed-moribund

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUND

Group 3 - Males

Animal #	Gross Findings, Tissue Masses	Other
4622		Lf. kidney-black; rt. kidney-pale; testes, sem. ves.-atrophied; external appearance-diarrhea.
4624*		Pit.-enlarged, dark; stomach-walls thickened; sem. ves.-small.
4628*	Lg. t.m.-lf. side head/neck.	Lungs-white spots; kidneys-cortex wide, pink striated zone; adrenal-lf. slightly enlarged; stomach-walls thick; animal had record of swelling of joints of rt. hind foot.
4629		Thyroid-enlarged; heart-enlarged; kidneys-enlarged, pale, pitted; adrenals-pale; testes-small.
4631		Lung-congested; kidneys-pelvis dilated; lf. side premaxilla swollen; lf. eye-discharge.
4637		Lung-rt. side dark red.
4639	Sm. t.m.-lf. abd. dorsal.	Red clot on brain; lungs-bright red; rt. maxillary abscess below rt. eye.
4641	Lg. t.m. (195gm) in abd. involving spleen, stomach, lf. kidney, lf. adrenal. Sm. t.m. (11gm) rt. head/neck.	Lungs-pale; liver-pale; spleen-slightly enlarged; red fluid in scrotal sacs.
4645	T.M.-chest, subcu. (72gm).	Heart-flaccid, slightly enlarged; liver-pale, margins rounded; spleen-enlarged; sem. ves.-slightly small.
5074	Sm. t.m. head/neck latero-ventral lf. side.	Liver-mottled.
5083		Heart-enlarged; liver-dark.
5085		NGF
5086		Liver-enlarged; thymus-enlarged; spleen-enlarged.
5089		Lung-dark brown, white spots on surface; liver-portion dark green in color.
[illegible]98		Liver-pale, 2 dark spots central lobe; lung-mottled; brain-2 nodules under brain, possible blood clots.

TABLE E

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUND

Group 3 - Males (contd)

Animal #	Gross Findings: Tissue Masses	Gross Findings: Other
5100	Hard mass in abd. cavity.	Lung-mottled; liver-enlarged, pale; testes-blood colored fluid in scrotum.
5103		Pit.-enlarged, dark red; lung-hem.; sem. ves.-enlarged.
5104	Sm. t.m. head/neck ventral filled with watery fluid.	Liver-pale; spleen-enlarged.
5109		Pit.-enlarged, pale; lung-dark red.
5119	Med. t.m.-ventral head/neck region.	Lung-congested.
5125	Sm t.m.-rt. fore legs.	Lung-abscessed; heart-encysted.
5126	Mass-rt. median liver lobe.	Lung-hem. with some nodules; liver-black spots.
5128	N.P.	
5131		Pit.-enlarged; thyroid-enlarged; lung-mottled; kidney-enlarged.
5133*		Brain-brown areas on surface; lung-yellow areas; heart-small; spleen-small; kidney-cortex wide, slightly pitted, pelvis slightly dilated, wide striated zone between cortex, medulla. Lg. in proportion to body weight; mes. lymph node-dark red in color; testes-small, flaccid.

*sacrificed-moribund

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUND

Group 4 - Males

Animal #	Gross Findings: Tissue Masses	Gross Findings: Other
4673		Lungs-dark red.
4676	Possible t.m. involving lf. thyroid.	Thyroid-enlarged; lungs-dark red, splotchy; adrenals-speckled.
4679		Thymus, spleen, mes. lymph nodes, kidney-enlarged; lungs-mottled, red with yellow; pancreas-nodular, dark; thyroid-dark; liver-yellow patches; bladder-full, appears blocked; rt. kidney-yellow mat.; testicles-purple, small; heart-flaccid; brain-dark area on surface; pit.-light area on surface.
4683		Brain-dark red with clot; lungs-dark red.
4685		Autolysis.
4687*		Testes, sem. ves.-atrophied.
4688	Sm. t.m.-rt. side head (9gm).	Lungs-splotchy; adrenals-triangular shape.
4690		Submax. sal.-enlarged; spleen-enlarged; rt. kidney-white, wedged spot-cortex; adrenal-slightly enlarged.
4693		Brain-clot; lungs-congested; kidneys-blistered, enlarged; testes, sem. ves.-atrophied; both rear feet-abscessed.
4694	T.M.-rt. side head	Lung-dark, white spots; rt. kidney-misaligned; testes-atrophied.
4696		Lungs-hem.; spleen-enlarged.
5223		Lungs-congested; adrenals-enlarged; heart-dark.
5224		Cannibalized.
5229		Brain-pale; pit-enlarged; kidneys-pale; thyroid-enlarged; liver-pale, enlarged; spleen-enlarged; testes-small.
5234		Lung-mottled.
5235		Lung-mottled.
5237	GI tract-more or less a t.m.	Liver-pale, enlarged; adrenals-pale, enlarged.

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUND

Group 4 - Males (contd)

Animal #	Gross Findings: Tissue Masses	Gross Findings: Other
5246		Brain-blood clot; lung-hem.
5249	Ulcerated mass-lat. side of head	Lung-abscessed; spleen-enlarged; kidney-irregular in shape with white nodular protrusions on surface, white areas extend into medulla.
5250	Ulcerated mass-lf. side head, involving lf. eye.	Lf. lung-contains fleshy mass; rt. lung-spongy area; liver-mottled; heart-rt. auricle distorted; spleen-enlarged, urinary bladder contains red fluid.
5251	Lg, t.m.-dorsal abd.. lf. side.	Lung-pale; liver-pale; small intestine contains yellow mucous.
5256		Lung-pale, dark red areas; Pit.-enlarge dark with red spots; kidneys-enlarged.
5257*		Pit.-enlarged, indented into brain; lung-mottled: liver-mottled; spleen-small; kidney-ulcerated lesion-left.
5265		Brain-dark red; liver-dark; pit.-dark; lung-mottled, med. lobe appears greatly enlarged, red.
5268*		Pit.-enlarged; stomach-contains yellowish-white mucous.
5277		Lung-mottled; liver-enlarged; adrenals-enlarged.
5283		Lung-mottled, congested, yellow nodules, yellow material inside; kidney-renal pelvis dilated; mes. lymph node-enlarged.
5284*		Pit.-enlarged.
5285		Lung-hem., congested; liver-enlarged; kidney-pale, enlarged.
5287		Lung-dark red all lobes. pinpoint yellow areas; brain-covered with red fluid.
5288		Pit.-enlarged, dark; lung-congested.
5292		Advanced autolysis.
5295		Lung-red blotchy areas; testes-very small.

*sacrificed-moribund

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUND

Group 1 - Females

Animal #	Gross Findings: Tissue Masses	Gross Findings: Other
4506	Sm. mass (16g) rt. pelvic, ventral; mass involving stomach, spleen, kid., adrenals, pancreas, liver, diaphragm.	Lungs-splotchy; liver-white spots; lf. side abd. distended, coffee colored fluid in abd. cavity.
4507	Mass (6gm) lf. pelvic, ventral; mass (28gm) rt. pelvic, ventral; mass (17gm) rt. thigh, ventral.	Heart-enlarged, pale; lungs-pale, mottled; liver-pale; spleen-greatly enlarged, misshapen; pit.-dark spot.
4509*		Stomach-app. irritated; pit.-enlarged.
4514	Sm. t.m. lf. ventral pelvic.	Lungs-dark red; liver-pale; rt. eye-abcess.
4516*	T.M. rt. ventral thorax (64gm); t.m. lf. side head/neck (26gm).	Spleen-enlarged; lf. adrenal-enlarged; rt. adrenal-small.
4517	T.M. rt. ventral pelvis (411gm)	Adrenals-enlarged, speckled.
4520	T.M. on adrenal?	Pit.-enlarged; lungs-congested.
4717		Adrenals-speckled; lungs-mottled, slightly enlarged.
4722	Lg. hard mass in abd. cavity.	Pit., adrenals, spleen-enlarged; Kid.-enlarged, black, pelvis dilated.
4723		Ovaries-enlarged, fluid-filled; liver-enlarged, mottled; lungs-mottled.
4725		Lf. ovary-cystic; lungs-mottled; pit.-greatly enlarged.
4729		Wasted; pit.-enlarged, dark; adrenals-speckled.
4737	Salivaries-enlarged mass-like, dark solid.	Lungs-deep red; spleen-enlarged, dark; adrenals-enlarged.
4738	Sm. t.m.-rt. pelvic ventral.	Lungs-dark red; lf. eye-red, scarred.
4739		Pit.-greatly enlarged, black; lungs-dark red; liver-dark red with light areas.
4742	Lg. t.m. (310gm) rt. abd. ventral-ulcerated.	Lungs-mottled; liver-slight enlarged; adrenals-enlarged,speckled; green mucous in GI tract; rt. ovary-red cyst.
4744		Pit.-greatly enlarged.
4757	Sm. t.m.-lf. thoracic cavity.	Pit.-greatly enlarged; slightly enlarged mes. lymph node; lungs-hemorrhagic; congested GI tract.

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUND

Group 1 - Females (contd)

Animal #	Gross Findings: Tissue Masses	Gross Findings: Other
4767		Pit.-greatly enlarged; adrenals-enlarged.
4769	Lg. t.m. (184gm) mammary, lf. pelvic ventral.	Active mammary tissue; lungs-congested; pit.-slightly enlarged.

*sacrificed-moribund

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUND

Group 2 - Females

Animal #	Gross Findings: Tissue Masses	Gross Findings: Other
4547	T.M.-rt. thorax (235gm).	Pit.-enlarged, red; lungs-pale with dark areas; liver-pale, pitted; spleen-enlarged; adrenals-enlarged, lf. speckled.
4555	Lg. mass-lwr. rt. part of body; sm. mass-upr. lf. part of body.	Pit.-enlarged, bloody filled; lung-red.
4559	T.M.-rt. ventral pelvis (306gm); t.m. head, neck, ventral (82gm).	Adrenals-appear enlarged.
4563*		Pit.-greatly enlarged.
4564	T.M.-lf. ventral pelvis (353gm).	Liver-indented by ribs; pancreas-thickened.
4568	T.M.-lf. cervical (18gm).	Lungs-orange.
4848*		Pit.-greatly enlarged; appears emaciated; diarrhea.
4852	Lg. mass (262gm)-pelvic.	Cannibalized.
4857	Lg. mass (nodular)involving heart/ lungs.	Eyes-filmed; thyroid-enlarged; lf. renal pelvis-dilated; pancreas dark; mes. lymph-enlarged, dark; uterus-dark.
4858	Sm. mass-mammary, pelvic.	Pit.-enlarged, white spots; spleen clear nodule; esophagus-impacted with food, bedding; adrenals-enlarged, white spots.
4861	Lg. t.m.-head, neck,ventral, ulcerated (393gm).	Stomach-greatly distended; mes. lymph node-enlarged, black; lungs-mottled; lf. adrenal-enlarged; liver,spleen-black.
4864	Sm. mass-rt. thoracic; t.m. inguinal.	Lumbar fat-yellow; lungs-hem.; liver-dark with black spots.
4873	Lg. t.m.-rt. ventral abd. (554gm).	Decomposed.
4874		Heart-appears small; lungs-nodules on all lobes.
4881		Pit.-enlarged.
4883		Pit.-enlarged, blood filled; thyroid-grey; lungs-nodules.
4884		Brain-pale, soft; pit.-enlarged; liver-pale; spleen-enlarged; lf. adrenal-enlarged.
4889		Pit.-enlarged.
4892	Subcu. thoracic t.m. (66gm).	Lungs-mottled, nodular; rt. adrenal-enlarged.
4893	T.M.-cecum (med.).	Abd. cavity-clear fluid; spleen-enlarged; renal pelvis-dilated; adrenals-white speckles; lungs-congested.

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUND

Group 2 - Females (contd)

Animal #	Gross Findings: Tissue Masses	Gross Findings: Other
4895		Pit.-enlarged; lungs-hem.; lf. ovary-cystic.
4899	Rt. adrenal, kidney-involved in mass.	Lungs-pale, nodular; liver-enlarged, blistered; spleen-enlarged, blistered; blood clot-like mass in lumbar fat.
4900		Pit.-enlarged, blood filled; lungs-mottled; liver-spotted; lf. adrenal-enlarged.
4901		Submax. gland-enlarged; lungs-pale, red fluid in chest cavity; lf. kidney-cystic, contains red fluid, blood clots; lf. adrenal-enlarged, adhered to kidney.
4904	T.M.-lf. side abd., med., ventral, ulcerated (78gm).	Pit.-enlarged greatly; adrenals-slightly enlarged.
4905	Sm. t.m.-ventral thorax.	Lungs-white nodules, congested; liver-lobes thickened, mottled; rt. uterine horn distended; pit., spleen-enlarged.
4908	Mammary mass-pelvic region.	Lungs-dark; lf. adrenal-enlarged.
4909		Pit.-greatly enlarged; lungs-congested; adrenals-speckled; lf. ovary-cystic.
4912	Rt. pelvic ventral-med.	Active mammary tissue; white nodule-rt. lobe of lung; lungs-mottled; lf. ovary-dark; lf. uterine horn-fluid filled; pit.-slightly enlarged.
4916	Med. t.m.-rt. abd., ventral, ulcerated (61gm).	Pit.-enlarged.
4920*	Sm. fatty nodule attached to sm. intestine.	Pit.-greatly enlarged; bloody fluid under brain; bleeding from orbital sinus; lungs-white nodules; liver-nutmeg; adrenals-dark, slightly enlarged, lf. slightly larger; red pinpoint areas-lining.

*sacrificed-moribund

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUND

Group 3 - Females

Animal #	Gross Findings: Tissue Masses	Gross Findings: Other
4597		Lung-black spots; possible accidental death-caught upper jaw in cage.
4601*		Pit.-greatly enlarged.
4604		Autolysis-advanced.
4610		Pit.-enlarged, dark; adrenals-enlarged, pale.
4613		Pit.-enlarged, dar red; lungs-dark red; active mammary tissue-inguinal.
4614*		Pit.-enlarged; active mammary glands.
4615		Accidental - no tissues.
4617		Pit.-enlarged, black; lungs-splotchy.
4997*		Pit.-enlarged, yellow and black areas; spleen-rough; kidneys-granular, enlarged, blistered, pale; adrenals-enlarged.
4999		Pit.-enlarged greatly; thyroid-enlarged.
5001*	Lg. t.m.-lf. side.	Heart-appears enlarged; liver-pale; spleen-pale, enlarged, margins rounded; stomach-contains red fluid; mes. lymph node-slightly enlarged.
5012		NGL
5014		Ext. vulva opening-closed; urinary bladder distended with blood colored urine; chest cavity, abd. cavity-clear red fluid; lungs-nodules; kidney-pelvis dilated; adrenals-enlarged.
5016		Pit.-greatly enlarged; liver-congested, mottled; adrenals-slightly enlarged, speckled; thickened rt. ear.
5021		Uterus-greatly distended with red fluid; mes. lymph node-dark.
5029*	T.M.-lf. pelvic, ventral (59gm).	Pit.-enlarged greatly; lungs-white nodules.
5031		Pit.-greatly enlarged; lungs-congested.

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUND

Group 3 - Females (contd)

Animal #	Gross Findings: Tissue Masses	Gross Findings: Other
5038	Lg. t.m.-lf. flank groin (524gm); dark objects lying near spine (sm.)	Rt. lung-mottled; liver-margins rounded, renal pelvis dilated; mes. lymph node-dark.
5042	Lg. t.m.-lf. abd. ventral (119gm).	Chest-cavity-clear red fluid; lungs-dark red; pancreas-serogelatinous fluid; ovary-cystic.
5043		Pit.-enlarged, black; lungs-hem; yellow mucous-GI tract.
5046		Pit.-enlarged, black spotted; lung-contains foam; aortic arch-thick, tough; kidney-pale, blistered; mes. lymph node-enlarged.
5048	Sm. t.m.-pelvic, ventral (4gm); both uterine horns-sm. masses (gravid appearance); rt. lobe liver-cyst-like mass.	Pit.-enlarged, dark; liver-grey, rt. lobe dark red.
5051	Lg. t.m. ventral rt. side, abd., (544gm).	Liver-enlarged, light pale; spleen-enlarged; kidneys-black marginal line at cortex, medullary areas; adrenals-enlarged.
5055	Pancreas-multinodular mass; liver-pale, several lobe mass; lf. ovary-mass.	Abd. cavity-filled with blood; stomach-enlarged; spleen-enlarged, pale; rt. ovary-cyst, large; kidneys-nodules; heart-nodules; lung-nodules; lf. adrenal-enlarged, dark; pit.-enlarged.
5056		Pit.-large, dark red; lungs-white splotches on surface,speckled with black spots; kidneys-pale, mottled; eyes-covered black crust.
5062	Mass-right pelvic.	Pit.-enlarged, spotted.
5063		Lung-one lobe white, other pale; liver-enlarged, mottled; kidney-pale, yellow inside; adrenals-lf. tumor; lg. intes.-nodule.
5064		Stomach-fluid filled; kidneys-pitted; liver-pale; lungs-yellow fluid; pit.-enlarged.
5070	Lg. mass-rt. pelvic.	Pit.-enlarged; liver-pale; spleen-enlarged; adrenals-enlarged.

*sacrificed-moribund

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUND

Group 4 - Females

Animal #	Gross Findings: Tissue Masses	Gross Findings: Other
4649	Dark mass on lung.	Chest cavity filled with blood.
4656	Lg. t.m. involving uterus body, cervix, vagina.	Pit.-enlarged; spleen-enlarged; stones in renal pelvis; adrenals-white speckles; bleeding from vulva.
4659		Pit.-enlarged; lungs-white spots, hem.
4660*		Pit.-enlarged; head-tilted.
4661*	Rt. pelvic ven.-t.m. (5gm); mammary mass-pelvis.	Pit.-enlarged; adrenal-enlarged, dark.
4662	Sm. mass-cervical ven. (6gm).	Pit.-enlarged; lungs-congested.
4665*	Sm. t.m.-lf. pelvic ven. (37gm).	Lungs-pale; liver-mottled; kidneys-mottled; submax. glands-enlarged.
4666		Pit.-light color; liver-mottled, margins rounded; spleen-enlarged; lf. kidney-pelvis dilated through medulla, contains yellow frothy material; adrenals-speckled; GI tract-adhesions.
4667	Sm. t.m.-ventral pelvic; t.m.-ventral, thoracic (6.5gm).	Lungs-dark splotches, brown; spleen-slightly enlarged; pit.-slightly enlarged.
4668		Pit.-enlarged; one ovary atrophied.
4669	T.M.-lf. side head (18gm).	Lungs-dark red.
4671		Pit.-enlarged; membranes-pale.
5149	Hard mass over left premaxillary.	Rt. uterus-enlarged, filled with red colored fluid.
5154		Pit.-enlarged, dark red; Adrenals-enlarged.
5157	Tissue mass ventral right side.	
5161		Cannibalized.
5163	Sm. t.m. right ventral pelvic region.	Lung-light colored; liver-pale; Adrenals-enlarged.
5169	Tissue mass left side axilla area ventral.	NGF
5173	Med. size mass abdominal cavity.	Lung-mottled; Pit.-enlarged; Spleen-enlarged.
5178	Sm. t.m. left thoracic region.	Lung-pale, abcess right lower lobe; liver-pale; spleen-enlarged; ovaries-cystic.

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUND

Group 4 - Females (contd)

Animal #	Gross Findings: Tissue Masses	Gross Findings: Other
5180		Cannibalized.
5183	Lg. t.m. left ventral cervical region. Sm. t.m. left thoracic region.	Lung-mottled; liver-pale.
5190	Lg. t.m. right abdominal region. Sm. t.m. left abdominal region. Rt. lobe of liver hard mass.	Lungs-mottled; liver-pale, enlarged, right lobe hard mass.
5192		Pit.-enlarged; lf. ovary-cystic.
5193		Pit.-enlarged; lung-congested; ovary-lf. encysted; lf. horn dark red in portions.
5198	Med. t.m.-lf. ventral pelvic region.	Liver-pale; pit.-enlarged.
5201		Liver-adhered to diaphragm, GI tract; rt. kidney-fused with liver; GI tract-fused ball-like mass; mes. lymph node-enlarged beads.
5203	Lg. t.m.-rt. ventral pelvic region (270gm).	Lungs-pale, white blotchy areas; adrenals-enlarged.
5204		Lung-congested; liver-pale; spleen-cannibalized.
5210		Adrenals-enlarged; cannibalized.
5212		Brain-pale, soft; rt. thyroid-pale, enlarged; lung-pale; liver-pale.
5216		Liver-mottled; ovaries-large, dark; thyroid-enlarged.
5218	Hard mass around rt. ovary (in capsules).	Pit.-enlarged, dark spot in center; lungs-mottled.

*sacrificed-moribund

PATHOLOGY

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Narrative Description

To facilitate review of microscopic findings, 4 sets of tables have been prepared on each experimental group of rats, including Male Controls, Male High Dose, Female Controls and Female High Dose groups.

The first set of tables is designated "Histological Findings" and lists abnormalities in each tissue that had been specified for microscopic examination from each rat examined. In addition, there is a listing of abnormalities found at necropsy in tissues other than those that had been specified for microscopic examination (unusual lesions).

The second set of tables is designated "Neoplasms" and gives a diagnostic classification of all neoplasms and preneoplastic alterations listed in the first set of tables.

The third set of tables is designated "Summary". The table referring to each experimental group consists of two parts, namely, "Summary - Histological Findings" and "Summary - Neoplasms". This set of tables provides information on the numbers of specific pathologic items in relation to the tissue count in the case of tissues that were specified for microscopic examination and in relation to the animal count in the case of lesions found at necropsy in tissues that had not been specified for microscopic examination. In selected instances, the tables also furnish information on the average numerical grade of lesion severity.

The fourth set of tables is designated "Incidence" and consists of two parts designated "Incidence - Non-neoplastic Abnormalities" and "Incidence - Neoplasms". The incidence of specific pathologic alterations and tumors are presented as a percentage of affected tissues or as a percentage of affected rats as appropriate.

A mortality table based on whether or not animals survived until the arbitrary date of sacrifice is also included.

There are two addenda to the tables. One is a tabulation of histological findings in animals in control and high dose groups that died from excessive heat on Day 76 of the study. The second is a tabulation of histological findings and neoplasms in animals that were examined after the main tables had been prepared. However, data in this addendum are included in summary and incidence tables.

Microscopic studies could not be reported on 10 animals because the tissues or animals were lost.

The following is a list by number and group assignment:

Group 1 - Female (Control)	Group 4 - Male (High Dose)	Group 4 - Female (High Dose)
4754	4679	4666
	5224	5157
	5234	5161
	5242	5180
	5245	

Comments on Diagnostic Terminology

(1) Myocardial fibrosis: This designation indicates any stage of a sequence of changes beginning with necrosis of occasional individual myocardial fibers and followed by loss of the affected fiber with collapse of the fibrous stroma (apparent fibrosis) and/or proliferation of stroma (real fibrosis). A variety of descriptive designations (including focal myocarditis and focal myocardial necrosis) could be applied to appropriate stages of the process, but the single designation "myocardial fibrosis" was chosen to simplify the tabulation of lesions.

(2) Hyaline globules in hepatic parenchymal cells: These "structures" varied in microscopic appearance from circumscribed eosinophilic cytoplasmic globules reminiscent of the eosinophilic globules described by Anderson et al.[1] in damaged rat livers to barely visible irregular hyaline areas that might be interpreted as collections of proteinaceous fluid within the cytoplasm of the affected hepatic cells. The degree of hepatic cell involvement was never more than slight, there was no evidence of associated hepatic cell damage, and the range of incidence (in test animals and controls) was not significant.

(3) Increased hemosiderin - spleen: Rats with heavy deposition of hemosiderin in the splenic pulp were noticed early in the process of microscopic examination. Since all spleens had microscopically demonstrable hemosiderin in varying amounts, an evaluation of increased hemosiderin over any selected norm was entirely subjective. However, observations recorded (in the incidence tables) suggest that female rats were more prone to increased hemosiderin in the spleen than males without significant differences between test animals and controls.

(4) Chronic inflammation - kidneys: This designation indicates the common "chronic nephritis" or "glomerulonephrosis" of rats. The term "chronic inflammation" has been specified for use in the carcinogenesis program and is used in this report in compliance with the prescribed nomenclature. The condition ranges in microscopic appearance from distention of renal corpuscles and associated tubules with proteinaceous fluid to eventual atrophy of glomeruli and tubules along with fibrosis.

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[1]Anderson, P.J., Cohen, S. and Barka, T.: Hepatic Injury. Archives of Pathology, Vol. 71, pp. 101/89 - 107/95 (1961).

(5) Calcinosis - kidneys: This designation refers to focal hematoxylinophilic concretions (focal mineralization) beneath the epithelium of the renal pelvis and to a lesser extent in the basement membrane of tubules in the renal medulla.

(6) Capillary ectasia - adrenals: This term refers to foci of capillary alteration in the adrenal cortex ranging from a marked dilation of adjacent capillaries to the development of intracapillary hematoma-like accumulations of blood to which the designation hematocyst might also be applied.

(7) Focal lipidosis - adrenals: This term refers to focal areas in the adrenal cortex containing a noticeable increase of lipid material as compared with adjacent cortex. The affected cortical cells were enlarged and the cytoplasm characteristically contained medium and large droplets of lipid material manifest in routine histologic preparations as medium and large cytoplasmic vacuoles. Developing foci of lipidosis were manifest as foci of moderate cell hypertrophy in which slight to moderate increase of lipid material was apparent.

Summary

The following notations are made from a non-statistical review of the tabular data.

There was a higher percentage of intercurrent deaths (natural deaths and moribund sacrifices) among male controls than male high dose animals. In the case of female animals the relationship was reversed, namely a lower percentage of intercurrent deaths among female controls than high dose females. Conclusions or impressions on survival are not warranted on these data alone and without statistical analysis.

Male rats had a higher incidence of myocardial fibrosis than females without relation to the compound tested.

Female rats had a higher incidence of increased hemosiderin in the spleen without relation to the compound tested.

Female rats had a higher incidence of increased hemopoiesis in the spleen without apparent relation to the compound tested.

Male rats had a higher incidence of chronic inflammation of the kidneys than females without relation to the compound tested.

Female rats had a higher incidence of renal calcinosis than males without relation to the compound tested.

Female rats had a higher incidence of capillary ectasia (hematocysts) in the adrenal cortex than males without relation to the compound tested.

With regard to abnormalities affecting C-cells in the thyroids, the sum of C-cell hyperplasias and C-cell adenomas in each experimental group was within the same numerical and/or percentage range. Differences in the incidence of either hyperplasia or adenoma among groups of rats may thus reflect pathologic interpretation more than actual differences in the state of C-cells in the various groups.

Visual review of the tabulated data on neuplasms did not indicate any compound-related effect on the incidence or pattern of tumors among the different groups of animals.

Conclusion

The degree and pattern of lesions and abnormalities seen in the organs of the control and test animals warrant a conclusion that they were unrelated to compound administration.

Submitted by:

H. R. Seibold, V.M.D.

KEY

d = Died or was killed *in extremis* before termination of experiment.

* = Indicates presence of neoplasm (benign and/or malignant). So-called preneoplastic liver lesions are included.

- = No significant monospecific alterations were seen.

+ = Tissue alteration as specified.

1 = Minimal

2 = Slight

3 = Moderate

4 = Well marked

5 = Severe

0 = Tissue not examined.

INCIDENCE - NON-NEOPLASTIC ABNORMALITIES

	Male		Female	
	Control	High Dose	Control	High Dose
Pituitary				
Abscess	2%		2%	
Cyst				2%
Massive necrosis	2%			
Thyroid				
C-cell hyperplasia	9%	2%	10%	6%
Follicular hyperplasia	1%			
Heart				
Myocardial fibrosis	20%	5%	5%	1%
Endocardial disease	1%	3%		
Bacterial endocarditis		3%		
Liver				
Hyaline globules	4%	6%	10%	5%
Fatty change	6%	3%	4%	2%
Passive congestion	2%	8%	1%	2%
Central necrosis	2%	5%	1%	6%
Reactive foci		1%		
Bile duct proliferation				1%
Increased hemosiderin				2%
Infarction				1%
Congenital cyst				1%
Spleen				
Increased hemosiderin	12%	8%	33%	35%
Increased hemopoiesis	1%	3%	9%	12%
Increased granulopoiesis				2%
Atrophy	4%	7%		
Reactive hyperplasia		4%		
Reticulosis	1%			
Kidneys				
Chronic inflammation	84%	78%	30%	23%
Calcinosis	1%	3%	25%	27%
Papillary necrosis	1%			
Metastatic abscesses		3%		
Suppurative pyelitis		1%	1%	2%
Interstitial nephritis				1%
Adrenals				
Capillary ectasia	5%	8%	64%	1%
Focal lipidosis	23%	21%	18%	20%
Cortical hemorrhage		1%		1%
Unilateral necrosis			1%	
Focal medullary hyperplasia			1%	

(continued)

INCIDENCE - NON-NEOPLASTIC ABNORMALITIES
(Continued)

	Male		Female	
	Control	High Dose	Control	High Dose
Pancreas				
Focal acinar atrophy	7%	6%	4%	4%
Pancreatitis			1%	
Stomach				
Ulcer	3%	1%		
Chronic inflammation				1%
Mucosal atrophy	1%			
Mucosal calcification		10%	1%	
Large Intestine				
Nematodiasis	9%	4%	7%	2%
Impaction	2%			
Chronic colitis				2%
Mesenteric Lymph Node				
Hematoma	2%			
Fibrosis	2%			
Lymphadentis		2%		
Lymphectasia			2%	
Reactive hyperplasia				3%
Increased pigmentation				5%
Urinary Bladder				
Urolith	2%			3%
Chronic ulcer			1%	
Cystitis	3%			3%
Testes				
Atrophy	11%	10%		
Ovaries				
Cyst			13%	15%
Bone Marrow				
Granulocytic hyperplasia	4%	12%		6%
Erythroid hyperplasia	3%		3%	1%
Decreased cellularity		2%		3%
Osteodystrophy	1%			
Lungs				
Alveolar histiocytosis	1%	3%	1%	6%
Bronchopneumonia	2%	1%		1%
Interstitial pneumonia		1%		
Murine pneumonia		1%		
Metastatic abscesses	1%			
Abscess				1%

(continued)

INCIDENCE - NON-NEOPLASTIC ABNORMALITIES
(Continued)

	Male		Female	
	Control	High Dose	Control	High Dose
Uterus				
Hydrometra			1%	
Endometria polyp				2%
Skeleton				
Periostitis		1%		
Multiple Distribution				
Polyarteritis	5%	3%	1%	
Metastatic calcification	6%	4%		
Focal granulomatosis	1%			
Chronic abscesses	1%			
Integument				
Pyogenic granuloma	1%			
Abscess		1%		
Mammary Gland				
Cystic hyperplasia			1%	
Chronic mastitis			1%	
Galactocele				4%
No Organ Specified				
Pyemia		1%		
Chronic abscess				2%
Acute peritonitis				1%
Chronic peritonitis				1%
Fat necrosis				1%
Types of lesions	41	38	28	43

SUMMARY

HISTOLOGICAL FINDINGS

Male - Control

	Average Numerical Grade of Lesion Severity	Incidence	Tissue Count
Pituitary			
Neoplasms		19	51
Massive necrosis		1	51
Abscess		1	51
Thyroids			
Neoplasms		1	77
C-cell hyperplasia		7	77
Follicular hyperplasia		1	77
Heart			
Myocardial fibrosis	(2)	16	82
Endocardial disease		1	82
Liver			
Neoplasms		4	82
Hyaline globules	(2)	3	82
Fatty change	(3.2)	5	82
Passive congestion		2	82
Central necrosis		2	82
Spleen			
Increased hemosiderin		10	81
Increased hemopoiesis		1	81
Reticulosis		1	81
Atrophy		3	81
Kidneys			
Chronic inflammation	(3)	68	81
Calcinosis	(3)	1	81
Congenital cyst		1	81
Papillary necrosis		1	81
Adrenals			
Neoplasms		5	79
Capillary ectasia	(1.6)	4	79
Focal lipidosis	(1.4)	18	79
Pancreas			
Neoplasms		2	71
Focal acinar atrophy	(1)	5	71

(continued)

SUMMARY

HISTOLOGICAL FINDINGS

Male - Control (Continued)

	Average Numerical Grade of Lesion Severity	Incidence	Tissue Count
Stomach			
Ulcer		2	78
Mucosal atrophy		1	78
Small Intestine		0	75
Large Intestine			
Nematodiasis		5	55
Impaction		1	55
Mesenteric Lymph Node			
Hematoma		1	53
Fibrosis		1	53
Urinary Bladder			
Urolith		1	61
Cystitis	(3)	2	61
Testes			
Neoplasms		5	80
Atrophy		9	80
Bone Marrow			
Granulocytic hyperplasia		3	77
Erythroid hyperplasia		2	77
Osteodystrophy		1	77

	Incidence	Animal Count
Lungs		
Neoplasms	2	83
Alveolar histiocytosis	1	83
Bronchopneumonia	2	83
Metastatic abcesses	1	83
Integument		
Neoplasms	1	83
Pyogenic granuloma	1	83
Multiple Distribution		
Polyarteritis	4	83
Metastatic calcification	5	83
Focal granulomatosis	1	83
Chronic abscesses	1	83

(continued)

SUMMARY

HISTOLOGICAL FINDINGS

Male - Control (Continued)

	Average Numerical Grade of Lesion Severity	Incidence	Animal Count
Mammary Gland			
Neoplasms		1	83
No Organ Specified			
Neoplasms		6	83
Soft Tissue			
Neoplasms		3	83
Parathyroid			
Neoplasms		2	83

SUMMARY

HISTOLOGICAL FINDINGS

Male - High Dose

	Average Numerical Grade of Lesion Severity	Incidence	Tissue Count
Pituitary			
Neoplasms		9	36
Thyroids			
Neoplasms		5	66
C-cell hyperplasia		1	66
Heart			
Myocardial fibrosis	(1.5)	4	76
Endocardial disease		2	76
Bacterial endocarditis		2	76
Liver			
Neoplasms		5	77
Hyaline globules	(1.8)	5	77
Fatty change	(3.5)	2	77
Passive congestion		6	77
Central necrosis		4	77
Reactive foci		1	77
Spleen			
Increased hemosiderin		6	76
Increased hemopoiesis		2	76
Atrophy		5	76
Reactive hyperplasia		3	76
Kidneys			
Chronic inflammation	(2.7)	59	76
Calcinosis	(2)	2	76
Metastatic abscesses		2	76
Suppurative pyelitis		1	76
Adrenals			
Neoplasms		5	73
Capillary ectasia	(1.5)	6	73
Focal lipidosis	(1.3)	15	73
Cortical hemorrhage		1	73
Focal medullary hyperplasia		1	73
Pancreas			
Focal acinar atrophy	(1.8)	4	70
Stomach			
Neoplasms		1	74
Mucosal calcification		1	74
Ulcer		1	74

(continued)

HISTOLOGICAL FINDINGS

Male - High Dose (Continued)

	Average Numerical Grade of Lesion Severity	Incidence	Tissue Count
Small Intestine		0	72
Large Intestine			
Nematodiasis		2	47
Mesenteric Lymph Node			
Lymphadenitis		1	52
Urinary Bladder		0	57
Testes			
Neoplasms		9	73
Atrophy		7	73
Bone Marrow			
Granulocytic hyperplasia		8	66
Decreased cellularity		1	66

	Incidence	Animal Count
Lung		
Tumors	1	77
Alveolar histiocytosis	2	77
Interstitial pneumonia	1	77
Murine pneumonia	1	77
Bronchopneumonia	1	77
Integument		
Neoplasms	3	77
Abscess	1	77
Multiple Distribution		
Polyarteritis	2	77
Metastatic calcification	3	77
Skeleton		
Periostitis	1	77
No Organ Specified		
Neoplasms	4	77
Pyemia	1	77
Soft Tissue		
Neoplasms	3	77
Salivary Gland		
Neoplasms	1	77
Parathyroid		
Neoplasms	1	77

SUMMARY

HISTOLOGICAL FINDINGS

Female - Control

	Average Numerical Grade of Lesion Severity	Incidence	Tissue Count
Pituitary			
Neoplasms		37	62
Abscess		1	62
Thyroids			
Neoplasms		1	67
C-cell hyperplasia		7	67
Heart			
Myocardial fibrosis	(1.5)	4	73
Liver			
Neoplasms		8	72
Hyaline globules	(2)	7	72
Fatty change	(3)	3	72
Passive congestion		1	72
Central necrosis		1	72
Spleen			
Increased hemosiderin		23	70
Increased hemopoiesis		6	70
Kidneys			
Chronic inflammation	(1.8)	22	73
Calcinosis	(1.6)	18	73
Suppurative pyelitis		1	73
Adrenals			
Neoplasms		1	73
Capillary ectasia	(2.7)	47	73
Focal lipidosis	(2)	13	73
Unilateral necrosis		1	73
Pancreas			
Neoplasms		1	69
Focal acinar atrophy	(1)	3	69
Pancreatitis		1	69
Stomach			
Mucosal calcification		1	71

(continued)

SUMMARY

HISTOLOGICAL FINDINGS

Female - Control (Continued)

	Average Numerical Grade of Lesion Severity	Incidence	Tissue Count
Small Intestine		0	68
Large Intestine			
Nematodiasis		4	58
Mesenteric Lymph Node			
Lymphectasia		1	43
Urinary Bladder			
Chronic ulcer		1	68
Ovaries			
Neoplasms		1	70
Cyst/s		9	70
Bone Marrow			
Erythroid hyperplasia		2	67
Lung			
Alveolar histiocytosis		1	73

	Incidence	Animal Count
Mammary Gland		
Neoplasms	25	73
Cystic hyperplasia	1	73
Chronic mastitis	1	73
Uterus		
Neoplasms	1	73
Hydrometra	1	73
Multiple Distribution		
Polyarteritis	1	73
Integument		
Neoplasm	2	73
No Organ Specified		
Neoplasm	6	73

SUMMARY

HISTOLOGICAL FINDINGS

Female - High Dose

	Average Numerical Grade of Lesion Severity	Incidence	Tissue Count
Pituitary			
Neoplasms		37	65
Cyst		1	65
Thyroids			
Neoplasms		4	68
C-cell hyperplasia		4	68
Heart			
Myocardial fibrosis	(2)	1	81
Liver			
Preneoplastic alterations		3	81
Neoplasms		2	81
Hyaline globules	(2)	4	81
Fatty change	(4)	2	81
Passive congestion		2	81
Central necrosis		5	81
Bile duct proliferation	(2)	1	81
Increased hemosiderin		2	81
Infarction		1	81
Congenital cyst		1	81
Spleen			
Increased hemosiderin		28	81
Increased hemopoiesis		10	81
Increased granulopoiesis		2	81
Kidneys			
Chronic inflammation	(1.5)	19	82
Calcinosis	(2.1)	22	82
Suppurative pyelitis		2	82
Interstitial nephritis		1	82
Congenital cyst		2	82
Adrenals			
Capillary ectasia	(2.7)	49	80
Focal lipidosis	(2)	16	80
Cortical hemorrhage		1	80
Pancreas			
Focal acinar atrophy	(1.7)	3	73

(continued)

SUMMARY

HISTOLOGICAL FINDINGS

Female - High Dose (Continued)

	Average Numerical Grade of Lesion Severity	Incidence	Tissue Count
Stomach			
Neoplasms		1	78
Chronic inflammation		1	78
Small Intestine		0	73
Large Intestine			
Nematodiasis		1	57
Chronic colitis		1	57
Mesenteric Lymph Node			
Reactive hyperplasia		1	37
Increased pigmentation		2	37
Urinary Bladder			
Cystitis	(3)	2	70
Urolith		2	70
Ovaries			
Cysts		11	73
Bone Marrow			
Erythroid hyperplasia		1	70
Granulocytic hyperplasia		4	70
Decreased cellularity		2	70

	Incidence	Animal Count
Lung		
Alveolar histiocytosis	5	82
Bronchopneumonia	1	82
Abscess	1	82
Mammary Gland		
Neoplasms	31	82
Galactocele	3	82
Uterus		
Neoplasms	3	82
Endometrial polyp	2	82
Thymus		
Neoplasms	1	82

(continued)

SUMMARY

HISTOLOGICAL FINDINGS

Female - High Dose (Continued)

	Average Numerical Grade of Lesion Severity	Incidence	Animal Count
No Organ Specified			
Neoplasms		4	82
Chronic abscess		2	82
Acute peritonitis		1	82
Chronic peritonitis		1	82
Fat necrosis		1	82
Integument			
Neoplasms		2	82
Soft Tissue			
Neoplasms		1	82

NEOPLASMS

Male - Control

	Benign Tumors		Malignant Tumors	
	Incidence	Tissue Count	Incidence	Tissue Count
Pituitary				
Adenoma	19	51		
Thyroids				
C-cell adenoma	1	77		
Liver - Preneoplastic Alterations				
Basophilic focus	1	82		
Eosinophilic focus	1	82		
Clear cell focus	1	82		
Liver - Neoplasms				
Hepatocellular carcinoma			1	82
Adrenals				
Cortical adenoma	1	79		
Pheochromocytoma	3	79		
Cortical carcinoma			1	79
Pancreas				
Islet cell adenoma	2	71		
Testes				
Interstitial cell tumor	5	80		
	Incidence	Animal Count	Incidence	Animal Count
Mammary Gland				
Adenocarcinoma			1	83
Lung				
Alveolar/bronchiolar adenoma	2	83		
No Organ Specified				
Malignant lymphoma			1	83
Multiple plasmacytoma			1	83
Myeloid leukemia			1	83
Carcinoma			1	83
Adenocarcinoma			1	83
Synovial sarcoma			1	83
Soft Tissue				
Fibroma	3	83		
Integument				
Squamous cell carcinoma			1	83
Parathyroid				
Adenoma	2	83		
Total (Less Preneoplastic Alterations)	38		10	

Comment: A total of 41/83 animals had one or more tumors.

SUMMARY

NEOPLASMS

Male - High Dose

	Benign Tumors		Malignant Tumors	
	Incidence	Tissue Count	Incidence	Tissue Count
Pituitary				
Adenoma	9	36		
Thyroids				
C-cell adenoma	5	66		
Liver - Preneoplastic Alterations				
Clear cell focus	1	77		
Liver - Neoplasms				
Neoplastic nodules	3	77		
Hepatocellular carcinoma			1	77
Adrenals				
Pheocnromocytoma	5	73		
Stomach				
Squamous papilloma	1	74		
Testes				
Interstitial cell tumor	9	73		
	Incidence	Animal Count	Incidence	Animal Count
Salivary Gland				
Mixed tumor	1	77		
Lung				
Alveolar/bronchiolar adenoma	1	77		
No Organ Specified				
Sarcoma			2	77
Lymphosarcoma			1	77
Carcinoma			1	77
Soft Tissue				
Fibroma	3	77		
Integument				
Squamous cell carcinoma			3	77
Parathyroid				
Adenoma	1	77		
Total (Less Preneoplastic Alterations)	38		8	

Comment: A total of 38/77 animals had one or more tumors.

SUMMARY

NEOPLASMS

Female - Control

	Benign Tumors		Malignant Tumors	
	Incidence	Tissue Count	Incidence	Tissue Count
Pituitary				
Adenoma	34	62		
Thyroids				
C-cell adenoma	1	67		
Liver - Preneoplastic Alterations				
Clear cell focus	1	72		
Basophilic focus	5	72		
Liver - Neoplasms				
Neoplastic nodule	1	72		
Hepatocellular carcinoma			1	72
Adrenals				
Cortical adenoma	1	73		
Pancreas				
Islet cell adenoma	1	69		
Ovaries				
Sarcoma			1	70
	Incidence	Animal Count	Incidence	Animal Count
Integument				
Basal cell carcinoma			1	73
Fibrosarcoma			1	73
Mammary Gland				
Fibroadenoma	20	73		
Adenocarcinoma			6	73
Uterus				
Leiomyoma	1	73		
No Organ Specified				
Sarcoma			2	73
Lymphosarcoma			1	73
Reticulum cell sarcoma			1	73
Malignant lymphoma			1	73
Myeloid leukemia			1	73
Total	59		16	

Comment: A total of 52/73 animals had one or more tumors.

SUMMARY

NEOPLASMS

Female - High Dose

	Benign Tumors		Malignant Tumors	
	Incidence	Tissue Count	Incidence	Tissue Count
Pituitary				
Adenoma	37	65		
Thyroid				
C-cell adenoma	4	68		
Liver - Preneoplastic Alterations				
Basophilic foci	3	81		
Liver - Neoplasms				
Neoplastic nodule	1	81		
Carcinoma			1	81
Stomach				
Squamous cell carcinoma			1	78
	Incidence	Animal Count	Incidence	Animal Count
Integument				
Fibroma	1	82		
Squamous cell carcinoma			1	82
Uterus				
Leiomyosarcoma			1	82
Adenocarcinoma			1	82
Carcinoma			1	82
Mammary Gland				
Adenoma	3	82		
Fibroadenoma	23	82		
Adenocarcinoma			7	82
Thymus				
Thymona	1	82		
No Organ Specified				
Sarcoma			1	82
Myelosarcoma			1	82
Malignant lymphoma			1	82
Adenocarcinoma			2	82
Soft Tissue				
Sarcoma			1	82
Total (Less Preneoplastic Alterations)	70		19	

Comment: A total of 61/82 animals had one or more tumors.

PROJECT #1400

MORTALITY

	Heat Deaths	52 Week Sacrifice	Natural Death and Moribund Sacrifice	Working Number	Terminal Sacrifice
Male Control	6	10	34 (41%)	84	50 (59%)
Male High Dose	8	10	33 (40%)	82	49 (64%)
Female Control	17	10	20 (77%)	73	53 (73%)
Female High Dose	4	10	33 (38%)	86	53 (62%)

ADDENDUM TO TABLES

LBI PROJECT #1400

Histological Findings

Heat Deaths

Group No.	1 - Male - Control						4 - Male - High Dose					
Animal No.	4805	4812	4813	4816	4838	4840	5240	5241	5243	5244	5247	5248
Pituitary	0	-	0	-	-	0	-	0	0	-	0	0
Thyroids	-	-	-	-	-	-	-	-	-	-	-	-
Heart	-	-	-	-	-	-	-	-	-	-	-	-
Liver	-	-	-	-	-	-	-	-	-	-	-	-
Spleen	-	-	-	-	-	-	-	-	-	-	-	-
Kidneys Calcinosis	-	-	-	-	-	-	-	-	-	-	-	-
Adrenals	-	-	-	-	-	-	-	-	-	-	-	-
Pancreas	-	0	-	0	-	-	-	-	-	-	-	-
Stomach	-	-	-	-	-	-	-	0	-	-	-	-
Small Intestine	-	-	-	-	-	-	-	-	0	-	-	-
Large Intestine	-	-	-	0	-	-	-	-	-	-	-	-
Mesenteric Lymph Node	-	-	-	-	-	-	-	-	0	-	-	-
Urinary Bladder	-	-	0	0	-	-	-	-	0	-	-	-
Ovaries/Testes	-	-	-	-	-	-	-	-	-	-	-	-
Bone Marrow	-	-	-	-	-	-	-	-	-	-	-	-

(continued)

ADDENDUM TO TABLES

LBI PROJECT #1400

Histological Findings

Heat Deaths
(continued)

Group No.	1 - Female - Control																4 - Female - High Dose			
Animal No.	4697	4698	4699	4705	4706	4707	4751	4752	4753	4755	4756	4759	4762	4763	4766	4768	5184	5186	5187	5188
Pituitary	0	0	-	-	0	-	-	-	0	0	-	-	0	-	0	0	-	-	0	-
Thyroids	-	-	-	-	0	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-
Heart	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Liver	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Spleen	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Kidneys	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Calcinosis									3											
Adrenals	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Pancreas	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Stomach	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Small Intestine	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Large Intestine	-	-	-	-	0	-	0	-	-	-	-	-	-	-	-	0	-	-	-	-
Mesenteric Lymph Node	0	-	-	0	0	0	0	-	-	-	-	0	-	-	-	0	0	0	-	-
Urinary Bladder	-	0	-	-	0	-	-	0	0	-	-	-	0	-	-	0	0	-	-	-
Ovaries/Testes	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Bone Marrow	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

ADDENDUM TO TABLES

LBI PROJECT # 1400

Histological Findings and Neoplasms

Group No.	1 - Male Control				4 - Male High Dose		1 - Female Control	4 - Female High Dose	
Animal No.	4524	4536	4779	4845	4257	5283	4/25	4659	5216
Tissue Findings									
Pituitary	0	-	-	-		-		0	-
Neoplasms (adenoma)					*		+		
Thyroids	0	-	-	-	-	-	-	-	-
Heart	-	-	-	-	-	-	-	-	-
Liver	-	-	-	-				-	-
Fatty change					3		3		
Passive congestion						+			
Central necrosis						1			
Spleen	-	-		-	-	-			
Increased hemosiderin							+	+	+
Atrophy			+						
Kidneys	-	-	-	-	-		-	-	-
Chronic inflammation						1			
Adrenals	-	-		-	-	-	-	-	
Capillary ectasia			1						
Cortical hemorrhage									+
Pancreas	0	0	-	-	-	-	-	-	-
Stomach	-	-	-	-		-	-	-	-
Ulcer					+				

(continued)

ADDENDUM TO TABLES

LBI PROJECT # 1400

Histological Findings and Neoplasms (Continued)

Group No.	1 - Male Control				4 - Male High Dose		1 - Female Control	4 - Female High Dose	
Animal No.	4524	4536	4779	4845	4257	5283	4725	4659	5216
Tissue Findings									
Small Intestine	0	-	-	-	-	-	-	-	-
Large Intestine	-	-	-	-	-	-	-	-	-
Mesenteric Lymph Node	-	-	0	-	-	0	-	0	-
Urinary Bladder		0	0	-	0	-	-	0	0
Cystitis	3								
Testes	-	-	-		-	-	N/A	N/A	N/A
Atrophy				+					
Ovaries	N/A	N/A	N/A	N/A	N/A	N/A		-	-
Cyst							+		
Bone Marrow	-		-	-	-		-	-	-
Granulocytic hyperplasis						+			
Osteodystrophy		+							
Lungs									
Bronchopneumonia						+			
Multiple Distribution									
Metastatic calcification		+							
No Organ Specified									
Neoplasm (malignant lymphoma)				*					

INCIDENCE - NEOPLASMS

	Male		Female	
	Control	High Dose	Control	High Dose
Pituitary				
Chromophobe adenoma	37%	25%	55%	57%
Thyroids				
C-cell adenoma	1%	8%	1%	6%
Thymus				
Thymoma	0	0	0	1%
Parathyroid				
Adenoma	3%	2%	0	0
Liver - Preneoplastic Alterations				
Basophilic focus	1%	0	7%	4%
Eosinophiic focus	1%	0	0	0
Clear cell focus	1%	1%	1%	0
Liver				
Neoplastic nodule	0	4%	1%	1%
Hepatocellular carcinoma	1%	1%	1%	0
Carcinoma	0	0	0	1%
Adrenals				
Cortical adenoma	1%	0	1%	0
Cortical carcinoma	1%	0	0	0
Pheochromocytoma	4%	7%	0	0
Stomach				
Squamous papilloma	0	1%	0	0
Squamous cell carcinoma	0	0	0	1%
Pancreas				
Islet cell adenoma	3%	0	1%	0
Testes				
Interstitial cell tumor	6%	12%	NA	NA
Ovaries				
Sarcoma	NA	NA	1%	0
Salivary Gland				
Mixed tumor	0	1%	0	0
Mammary Gland				
Adenoma	0	0	0	4%
Fibroadenoma	0	0	27%	28%
Adenocarcinoma	1%	0	8%	9%
Lung				
Alveolar/bronchiolar adenoma	2%	1%	0	0

(continued)

INCIDENCE - NEOPLASMS
(continued)

	Male		Female	
	Control	High Dose	Control	High Dose
Integument				
Squamous cell carcinoma	1%	4%	0	1%
Basal cell carcinoma	0	0	1%	0
Fibrosarcoma	0	0	1%	0
Fibroma	0	0	0	1%
Soft Tissue				
Fibroma	4%	4%	0	0
Sarcoma	0	0	0	1%
Uterus				
Leiomyoma	NA	NA	1%	0
Leiomyosarcoma	NA	NA	0	1%
Adenocarcinoma	NA	NA	0	1%
Carcinoma	NA	NA	0	1%
No Organ Specified				
Sarcoma	0	3%	3%	1%
Lymphosarcoma	0	1%	1%	0
Reticulum cell sarcoma	0	0	1%	0
Myelosarcoma	0	0	0	1%
Synovial cell sarcoma	1%	0	0	0
Malignant lymphoma	1%	0	1%	1%
Myeloid leukemia	1%	0	1%	0
Multiple plasmacytoma	1%	0	0	0
Carcinoma	1%	1%	0	0
Adenocarcinoma	1%	0	0	2%
SUMMARY OF INCIDENCE				
Rats with one or more tumors	49%	49%	71%	74%
Tumors benign	79%	83%	79%	79%
Tumors malignant	21%	17%	21%	21%
Rats with one or more mammary tumors	1%		33%	38%
Mammary tumors benign	0%		77%	79%
Mammary tumors malignant	100%		23%	21%
Rats with malignant mammary tumors	1%		8%	9%
Number of rats with two types mammary tumor			2	2
Rats with mammary tumors having two types of tumor			8%	6%
Types of tumors	18	14	17	19
Benign tumors ÷ rats	46%	49%	80%	85%
Malignant tumors ÷ rats	12%	10%	22%	23%
Total tumors ÷ rats	58%	60%	103%	109%

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Male - Control																				
Animal No.	4522	4523	4525	4526	4527	4528[d]	4529	4530	4531	4532[d]	4533	4534[d]	4535	4537	4538	4539	4540	4541[d]	4542	4543
Tissue Findings																				
Pituitary	0	-	0	-	0		-	0	-	0	0	0	0	0			0	0	0	-
Neoplasms						*									*	*				
Massive Necrosis																				
Abscess																				
Thyroids	-		-	-	-	-	0	-	-	-	-	-	-		-	-	-	0	-	-
Neoplasms																				
C-cell hyperplasia		+												+						
Follicular hyperplasia																				
Heart	-	-		-	-		-	-	-	-		-	-			-	-	-	-	-
Myocardial fibrosis			1								1			2	1					
Endocardial disease						+														
Liver	-			-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Neoplasms		*	*																	
Hyaline globules																				
Fatty change																				
Passive congestion																				
Central necrosis																				
Spleen	-	-	-	-	-		-	-	-	-	-	-	-	-	-		-	0	-	-
Increased hemosiderin						+										+				
Increased hemopoiesis																				
Reticulosis																				
Atrophy																				

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Male - Control (Continued)																			
Animal No.	4522	4523	4525	4526	4527	4528[d]	4529	4530	4531	4532[d]	4533	4534[d]	4535	4537	4538	4539	4540	4541[d]	4542	4543
Tissue Findings																				
Kidneys																				
Chronic inflammation	4	3	2	4	2	2	4		3	5	3	3	1	4	3	3	1	2	3	3
Calcinosis									3											
Congenital cyst																				
Papillary necrosis																				
Adrenals		-	-		-	-		-	-	-	-	-	-	-	-		-	0		-
Neoplasms																				
Capillary ectasia	2																			
Focal lipidosis				2			1									1			2	
Pancreas	-	0	-	-	-	0	-	-	-	-		0		-	-		-	0	-	
Neoplasms																				
Focal acinar atrophy											1		1			1				1
Stomach	-	-	-	-	-	-	-	-	-	-	0	-	-	-	0	-	-	-	-	-
Ulcer																				
Mucosal atrophy																				
Small Intestine	-	-	-	-	-	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-
Large Intestine	0	0	-	-	-	-	-	-	0	-	0	-	-		-		0	-	-	0
Nematodiasis														+		+				
Impaction																				
Mesenteric Lymph Nodes	-	0	-	-	-	-	0	-	-	-	0	0	0	0	-	-	0	-	-	0
Hematoma																				
Fibrosis																				

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Male - Control (Continued)																				
Animal No.	4522	4523	4525	4526	4527	4528[d]	4529	4530	4531	4532[d]	4533	4534[d]	4535	4537	4538	4539	4540	4541[d]	4542	4543
Tissue Findings																				
Urinary Bladder	0	-	-	-	-	-	-	-	-	-	0	0	-	-	-	-	-	-	-	-
Urolith																				
Cystitis																				
Testes	-	-	-	-	-	-	-	-	-		-	-		-	-		-	-	-	-
Neoplasms													•							
Atrophy										•						•				
Bone Marrow	-	-	-	-	-	-	-	0	-	-	-	-		-	-	0	-	-	-	-
Granulocytic hyperplasia													•							
Erythroid hyperplasia																				
Lung																				
Neoplasms									•											
Alveolar histiocytosis																				
Bronchopneumonia																				
Metastatic abscesses																				
Integument																				
Neoplasms																				
Pyogenic granuloma																				
Multiple Distribution																				
Polyarteritis				•											•					
Metastatic calcification																				
Focal granulomatosis																				
Chronic abscesses																				

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Male - Control (Continued)
Animal No.	4522 4523 4525 4526 4527 4528[d] 4529 4530 4531 4532[d] 4533 4534[d] 4535 4537 4538 4539 4540 4541[d] 4542 4543
Tissue Findings	
Mammary Gland	
Neoplasms	
No Organ Specified	
Neoplasms	
Soft Tissue	
Neoplasms	
Parathyroid	
Neoplasms	

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Male - Control (Continued)																				
Animal No.	4544	4545	4546	4773	4774[d]	4776[d]	4777	4778[d]	4780[d]	4782	4783[d]	4785	4786[d]	4788	4791[d]	4792	4794	4795[d]	4797[d]	4798[d]
Tissue Findings																				
Pituitary	-	-	-	0	-	0	0	*	-	0	0	-	*	0	-	0	*	0	*	*
Neoplasms																				
Massive necrosis																				
Abscess																				
Thyroids	-	-		-	-	-	-	-	-	-	-	-	-	0	-	*		0	-	-
Neoplasms																	*			
C-cell hyperplasia			+																	
Follicular hyperplasia																				
Heart	-	-	-	-	-			-	-	-	-	-		-	-		-	-	0	
Myocardial fibrosis						3	2						3			2				2
Endocardial disease																				
Liver	-	0	-	-	-	-					-	-	-	-	-	-	-	-		
Neoplasms							*													
Hyaline globules										2										
Fatty change								3	3											
Passive congestion																			+	
Central necrosis																				4
Spleen	-	-	-	-	-		-	-	-	-	-	-	-	-	-	-	-	-	-	-
Increased hemosiderin						+														
Increased hemopoiesis																				
Reticulosis																				
Atrophy																				

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Male - Control (Continued)																				
Animal No.	4544	4545	4546	4773	4774[d]	4776[d]	4777	4778[d]	4780[d]	4782	4783[d]	4785	4786[d]	4788	4791[d]	4792	4794	4795[d]	4797[d]	4798[d]
Tissue Findings																				
Kidneys																		-	0	
Chronic inflammation	3	3	3	3	4	5	1	2	2	2	2	1		4	1	1	3			4
Calcinosis																				
Congenital cyst																				
Papillary necrosis													+							
Adrenals	-	-			-	-			-	-	-		-		0	-		-	-	-
Neoplasms				*																
Capillary ectasia							2										1			
Focal lipidosis			1				1	2				1		1			1			
Pancreas	-	-	-	-	-	0	-	0	-			-	0	-	-	-	-	-	-	-
Neoplasms										*	*									
Focal acinar atrophy																				
Stomach	-	-	-	-	-	-	-	0	-	-	-	-	-	-	-	0	-	-	-	-
Ulcer																				
Mucosal atrophy																				
Small Intestine	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	-	-
Large Intestine	0	0	-	0	-	-	0	-	-	0	-		-	-	-	-	-	0	-	-
Nematodiasis												+								
Impaction																				
Mesenteric Lymph Nodes	0	-	-	0	-		0	-	-	0	-	-	-	-	-	-	-	0	0	-
Hematoma						+														
Fibrosis																				

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Male - Control (Continued)																				
Animal No.	4544	4545	4546	4773	4774[d]	4776[d]	4777	4778[d]	4780[d]	4782	4783[d]	4785	4786[d]	4788	4791[d]	4792	4794	4795[d]	4797[d]	4798[d]
Tissue Findings																				
Urinary Bladder	-	-	-	-	-	-		-	-	0	-	-		-	-	0	-	0	0	-
Urolith							+													
Cystitis													3							
Testes	-	0	-	-	-	-	-	-	-		-	-	-	-		-	-	-		-
Neoplasms										+										
Atrophy															+				+	
Bone Marrow	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Granulocytic hyperplasia																				
Erythroid hyperplasia																				
Lung																				
Neoplasms							+													
Alveolar histiocytosis															+					
Bronchopneumonia																				
Metastatic abscesses																				
Integument																				
Neoplasms																				
Pyogenic granuloma		+																		
Multiple Distribution																				
Polyarteritis					+															
Metastatic calcification						+							+					+		
Focal granulomatosis																				
Chronic abscesses																				

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Male - Control (Continued)
Animal No.	4544 4545 4546 4773 4774[d] 4776[d] 4777 4778[d] 4780[d] 4782 4783[d] 4785 4786[d] 4788 4791[d] 4792 4794 4795[d] 4797[d] 4798[d]
Tissue Findings	
Mammary Gland	
Neoplasms	
No Organ Specified	
Neoplasms	
Soft Tissue	
Neoplasms	
Parathyroid	
Neoplasms	

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Male - Control (Continued)																				
Animal No.	4800	4801	4803[d]	4804	4806	4807	4808[d]	4809	4810	4811	4814	4815[d]	4817	4818[d]	4819[d]	4820[d]	4821	4822	4823[d]	4824[d]
Tissue Findings																				
Pituitary	0	-		-	0	-		-					-			0	-	-		
Neoplasms			+				+		+	+		+		+	+				+	+
Massive Necrosis											+									
Abscess																				
Thyroids	-	-		-	-	-	-	-	-				-	-	-	-	-	-	-	-
Neoplasms																				
C-cell hyperplasia			+							+	+									
Follicular hyperplasia												+								
Heart	-	-		-	-	-		-		-	-	-	-		-	-	-	-		-
Myocardial fibrosis			2				3		2					2					3	
Endocardial disease																				
Liver	-	-		-	-	-	-	-		-	-	-	-	-				-		-
Neoplasms									*											
Hyaline globules																	2			
Fatty change			4												3				3	
Passive congestion																				
Central necrosis																1				
Spleen	-	-			-	-	-	-	-	-			-			-	-	-		
Increased hemosiderin			+	+								+		+					+	
Increased hemopoiesis																				
Reticulosis																				
Atrophy															+					+

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Male - Control (Continued)																				
Animal No.	4800	4801	4803[d]	4804	4806	4807	4808[d]	4809	4810	4811	4814	4815[d]	4817	4818[d]	4819[d]	4820[d]	4821	4822	4823[d]	4824[d]
Tissue Findings																				
Kidneys					-										-					-
Chronic inflammation	4	4	3	2		4	4	1	3	2	5	4	3	4		3	4	3	2	
Calcinosis																				
Congenital cyst																				
Papillary necrosis																				
Adrenals	-	0		-	-			-	-	-		-	-	-	-	-		-	-	
Neoplasms											*									
Capillary ectasia																				
Focal lipidosis			1			1	2										1			1
Pancreas	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		-	-	-
Neoplasms																				
Focal acinar atrophy																	1			
Stomach	-	-		-	-	-	-	-	-	-	-	-	-	-		-	-	-	-	-
Ulcer			+												+					
Mucosal atrophy																				
Small Intestine	-	-	-	-	-	-	-	-	-	-	-	-	-	0	-	-	-	-	-	-
Large Intestine	0	0	-	-	-	0	-	0	-	-	-		0	-	-	-	-	0	-	-
Nematodiasis												+								
Impaction																				
Mesenteric Lymph Nodes	0	-	-	-	-	-	-	-	0	-	-	0	0	0	-	-	-	-	-	-
Hematoma																				
Fibrosis																				

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Male - Control (Continued)																				
Animal No.	4800	4801	4803[d]	4804	4806	4807	4808[d]	4809	4810	4811	4814	4815[d]	4817	4818[d]	4819[d]	4820[d]	4821	4822	4823[d]	4824[d]
Tissue Findings																				
Urinary Bladder	0	-	-	0	0	-	-	-	-	0	-	-	-	-	-	-	-	-	0	-
Urolith																				
Cystitis																				
Testes	-	-	-	-		-		-	-	-	-		-	-	-	-	-	-		-
Neoplasms					*		*													
Atrophy												+							+	
Bone Marrow	-	0	-	0	-	-	-	-	-	-		-	-	-	-	-	-	-	-	-
Granulocytic hyperplasia											+									
Erythroid hyperplasia																				
Lung																				
Neoplasms																				
Alveolar histiocytosis													+							
Bronchopneumonia			+																	
Metastatic abscesses																				
Integument																				
Neoplasms																				
Pyogenic granuloma																				
Multiple Distribution																				
Polyarteritis																				
Metastatic calcification																				
Focal granulomatosis					+															
Chronic abscesses											+									

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Male - Control (Continued)
Animal No.	4800 4801 4803[d] 4804 4806 4807 4808[d] 4809 4810 4811 4814 4815[d] 4817 4818[d] 4819[d] 4820[d] 4821 4822 4823[d] 4824[d]
Tissue Findings	
Mammary Gland	
Neoplasma	
No Organ Specified	
Neoplasms	
Soft Tissue	
Neoplasms	
Parathyroid	
Neoplasms	

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Male - Control (Continued)																				
Animal No.	4825[d]	4826[d]	4827[d]	4828	4829[d]	4830	4831	4832[d]	4833	4834	4835	4836[d]	4837	4839	4841[d]	4842	4843[d]	4844	4846
Tissue Findings																			
Pituitary	-		0	-		-	0	-	0		0	0	0	-	-	0	0	-	-
Neoplasms		*								*									
Massive necrosis																			
Abscess					+														
Thyroids	-	-	-	-	-	-	-	-	-	-	-	0	-	-	-	-	-	-	-
Neoplasms																			
C-cell hyperplasia	*																		
Follicular hyperplasia																			
Heart	-	-	-		-	-	-	-	-	-	-	-	-	-	-	-	-		-
Myocardial fibrosis				2														2	
Endocardial disease																			
Liver	-	-	-		-	-	-	-	-	-	-		-	-	-	-	-	-	-
Neoplasms																			
Hyaline globules				2															
Fatty change																			
Passive congestion												+							
Central necrosis																			
Spleen	-	-	-	-	-		-		-	-	-	-	-			-	0	-	-
Increased hemosiderin						+									+				
Increased hemopoiesis								+											
Reticulosis														+					
Atrophy																			

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Male - Control (Continued)																			
Animal No.	4825[d]	4826[d]	4827[d]	4828	4829[d]	4830	4831	4832[d]	4833	4834	4835	4836[d]	4837	4839	4841[d]	4842	4843[d]	4844	4846
Tissue Findings																			
Kidneys	-					0		-				-							
Chronic inflammation		2	3	4	4		4		3	3	1		3	3	2	2	5	3	3
Calcinosis																			
Congenital cyst										+									
Papillary necrosis																			
Adrenals	-		-		-	-		-	-		-	0	-	-		0	-	-	
Neoplasms		+		+			+												
Capillary ectasia																			
Focal lipidosis										3					2				1
Pancreas	-	-	0	-	-	-	-	-	-	-	-	-	-	-	-	0	0	-	-
Neoplasms																			
Focal acinar atrophy																			
Stomach	-	-		-	-	-	-	-	-	-	-	-	-	-	-	-	0	-	-
Ulcer																			
Mucosal atrophy			+																
Small Intestine	-	-	-	-	-	-	-	0	-	-	0	0	-	-	-	-	0	-	-
Large Intestine		-	-	0	-	-	-	-	0	0	0	0	0	0		0	0	-	0
Nematodiasis	+																		
Impaction															+				
Mesenteric Lymph Nodes	-	0		0	-	0	0	0	-	-	0	0	-	0	-	0	0	-	-
Hematoma																			
Fibrosis			+																

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Male - Control (Continued)																			
Animal No.	4825[d]	4826[d]	4827[d]	4828	4829[d]	4830	4831	4832[d]	4833	4834	4835	4836[d]	4837	4839	4841[d]	4842	4843[d]	4844	4846
Tissue Findings																			
Urinary Bladder	0	-	-	-	-	0	-	-	0	-	0	0	-	-	0	-	0	-	0
Urolith																			
Cystitis																			
Testes		-	-	-		-	-	-	-		-	-	-	-	0	-	0	-	-
Neoplasms										+									
Atrophy	+				+														
Bone Marrow	-	-		-		-	-		-	-	-	-	0	-	-	-	-	-	0
Granulocytic hyperplasia					+														
Erythroid hyperplasia			+					+											
Lung																			
Neoplasms																			
Alveolar histiocytosis																			
Bronchopneumonia																			
Metastatic abscesses					+														
Integument																			
Neoplasms			+																
Pyogenic granuloma																			
Multiple Distribution																			
Polyarteritis										+									
Metastatic calcification			+																
Focal granulomatosis																			
Chronic abscesses																			

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Male - Control (Continued)
Animal No.	4825[d] 4826[d] 4827[d] 4828 4829[d] 4830 4831 4832[d] 4833 4834 4835 4836[d] 4837 4839 4841[d] 4842 4843[d] 4844 4846
Tissue Findings	
Mammary Gland	
Neoplasms	
No Organ Specified	
Neoplasms	
Soft Tissue	
Neoplasms	
Parathyroid	
Neoplasms	

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	4 - Male - High Dose																								
Animal No.	4672	4673[d]	4674	4675	4677	4678	4680	4681	4682	4683[d]	4684	4685[d]	4686	4687[d]	4688[d]	4689	4690[d]	4691	4692	4693[d]	4694[d]	4695	4696[d]	5223[d]	5226
Tissue Findings																									
Pituitary	0		0	0	-	-	0	0	-	0	0	-	0		0	0	-	0	0	0	-	0	-	-	-
Neoplasms		*												*											
Thyroids	-	-	-	-		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0
Neoplasms																			•						
C-cell hyperplasia					2																				
Heart	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		-	-	-	-	-	-	-	-
Myocardial fibrosis				1									1												
Endocardial disease																									
Bacterial endocarditis		-															+								
Liver	-	-	-		-	-	-	-	-		-		-		-	-	-	-	-	-	-		-	-	-
Neoplasms				*																		*			
Hyaline globules																									
Fatty change																									
Passive congestion												+													
Central necrosis										+															
Reactive foci														3											
Spleen	-		-	-	-	-	-	-	-	-	-		-	-		-		-	-	-					-
Increased hemosiderin															+						+		+		
Increased hemopoiesis																								+	
Atrophy		+										+													
Reactive hyperplasia																	+					+			

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	4 - Male - High Dose (Continued)																								
Animal No.	4672	4673[d]	4674	4675	4677	4678	4680	4681	4682	4683[d]	4684	4685[d]	4686	4687[d]	4688[d]	4689	4690[d]	4691	4692	4693[d]	4694[d]	4695	4696[d]	5223[d]	5226
Tissue Findings																									
Kidneys	-		-								-	-		-									-		
Chronic inflammation	2	2	2	3	4	4	1	2	3	2			4		3	1		3	1	5		2		3	2
Calcinosis			2														+								
Metastatic abscesses																					2				
Suppurative pyelitis																									
Adrenals		-	-	-	-	-	-		-	-	-	-	-		-			-			-		-		-
Neoplasms	*																								
Capillary ectasia														1					1						
Focal lipidosis								1								1				1		2		1	
Cortical hemorrhage																	+								
Focal medullary hyperplasia																									
Pancreas	-	0		-	-		0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Focal acinar atrophy			3			2										1									
Stomach	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Neoplasms																									
Mucosal calcification																									
Small Intestine	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	-
Large Intestine	-	-	0	0	0	-	-	-	0	-	-	-	0	-	-	-	-	0	-	-	-	0	-	-	-
Nematodiasis																									
Mesenteric Lymph Node	-	-	-	0	-	0	-	-	-	-	0	-	-	-	0	-		-	-	-	0	-	-	0	-
Lymphadenitis																	+								

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	4 - Male - High Dose (Continued)																								
Animal No.	4672	4673[d]	4674	4675	4677	4678	4680	4681	4682	4683[d]	4684	4685[d]	4686	4687[d]	4688[d]	4689	4690[d]	4691	4692	4693[d]	4694[d]	4695	4696[d]	5223[d]	5226
Tissue Findings																									
Urinary Bladder	0	0	-	0	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Testes	-	-	-	-		-	-	-		0	-	-	-		0	-	-	-	-		-	-	-	-	-
Neoplasms					•				•																
Atrophy														•						•					
Bone Marrow	-		0	-	-	-	-	-	-	0	-	-	-	-		-		-	-				-	-	-
Granulocytic hyperplasia															•		•			•	•	•			
Decreased cellularity		•																							
Lung																									
Neoplasms																									
Alveolar histiocytosis		•																							
Interstitial pneumonia																	•								
Murine pneumonia																									
Integument																									
Neoplasms															•						•				
Abscess																									
Multiple Distribution																									
Polyarteritis																				•					
Metastatic calcification																				•				•	

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	4 - Male - High Dose (Continued)
Animal No.	4672 4673[d] 4674 4675 4677 4678 4680 4681 4682 4683[d] 4684 4685[d] 4686 4687[d] 4688[d] 4689 4690[d] 4691 4692 4693[d] 4694[d] 4695 4696[d] 5223[d] 5226
Tissue Findings	
Skeleton	
Periostitis	
No Organ Specified	
Neoplasms	
Pyemia	
Parathyroid	
Neoplasms	
Soft Tissue	
Neoplasms	
Salivary Gland	
Neoplasms	

TWO-YEAR TOXICITY STUDY IN RATS

IBT PROJECT #1400

Histological Findings

Group No.	4 - Male - High Dose (Continued)																								
Animal No.	5227	5229[d]	5230	5232	5233	5235[d]	5236	5237[d]	5238	5239	5246[d]	5249[d]	5250[d]	5251[d]	5253	5254	5255	5259	5260	5261	5262	5263	5265[d]	5266	5268[d]
Tissue Findings																									
Pituitary	0		-	0	0	0	-	0	-	0	0	0	0	-	0	-	0	0		0		0	-	0	
Neoplasms		*																	*		*				*
Thyroids	-		-	-	-	0	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Neoplasms		*																							
C-cell hyperplasia																									
Heart	-	-	-	-	-		-	-	-	-		0		-	-	-	-	-	-	-	-	-	-	-	-
Myocardial fibrosis						2																			
Endocardial disease											+														
Bacterial endocarditis													+												
Liver	-	-	-	-	-	-	-	-	-	-	-	-	-		-	-		-	-	-		-			-
Neoplasms																	2							1	
Hyaline globules																					4				
Fatty change																							+		
Passive congestion														+											
Central necrosis																									
Reactive foci																									
Spleen	-		-	-	-	-	-	-		-	-			-	-	-	-	-	-			-	-	-	
Increased hemosiderin									+												+				+
Increased hemopoiesis		+										+													
Atrophy																									
Reactive hyperplasia													+												

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	4 - Male - High Dose (Continued)																											
Animal No.	5227	5229[d]	5230	5232	5233	5235[d]	5236	5237[d]	5238	5239	5246[d]	5249[d]	5250[d]	5251[d]	5253	5254	5255	5259	5260	5261	5262	5263	5265[d]	5266	5268[d]
Tissue Findings																									
Kidneys												0													
Chronic inflammation	3		2	3	1		3		4	3	3			1	2	3	3	1	3	4	4		3	1	3
Calcinosis																			2						
Metastatic abscesses													1												
Suppurative pyelitis																									
Adrenals																									
Neoplasms	*																			*					
Capillary ectasia							2		2													2			
Focal lipidosis																1	1	1		2	1	2			2
Cortical hemorrhage																									
Focal medullary hyperplasia																									
Pancreas	-	-	-	-	-	-	-	0	-	-	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-
Focal acinar atrophy																	0								
Stomach	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Neoplasms																									
Mucosal calcification																									
Small Intestine	-	0	-	-	-	-	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Large Intestine	0	0	-	0	-	-	0	0	0	-	-	-	-	-	0	-	0	0	-	-	0	-	-	0	-
Nematodiasis																									
Mesenteric Lymph Node	-	0	-	-	-	-	0	0	-	0	-	-	-	-	0	-	0	-	0	-	-	-	-	-	-
Lymphadenitis																									

TWO-YEAR TOXICITY STUDY IN RATS

CBI PROJECT #1400

Histological Findings

Group No.	4 - Male - High Dose (Continued)																								
Animal No.	5227	5229[d]	5230	5232	5233	5235[d]	5236	5237[d]	5238	5239	5246[d]	5249[d]	5250[d]	5251[d]	5253	5254	5255	5259	5260	5261	5262	5263	5265[d]	5266	5268[d]
Tissue Findings																									
Urinary Bladder	0	-	-	0	-	-	-	-	0	0	-	0	-	-	-	-	-	-	0	0	0	-	-	0	-
Testes			-	-				-	-	-	-	-	-	-	0	-	-	-	-	-	-	-	-	-	-
Neoplasms	*					*	*																		
Atrophy		+			+																				
Bone Marrow	-	-	-	0	-	-	-	-	0	-	-	0		-	-	-	-	-	0		-	-	-	0	-
Granulocytic hyperplasia													+							+					
Decreased cellularity																									
Lung																					*				
Neoplasms																									
Alveolar histiocytosis																									
Interstitial pneumonia																									
Murine pneumonia																									
Integument												*													
Neoplasms																									
Abscess		+																							
Multiple Distribution																									
Polyarteritis																									
Metastatic calcification																									

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	4 - Male - High Dose (Continued)																							
Animal No.	5227	5229[d]	5230	5232	5233	5235[d]	5236	5237[d]	5238	5239	5246[d]	5249[d]	5250[d]	5251[d]	5253	5254	5255	5259	5260	5261	5262	5263	5265[d]	5266	5268[d]
Tissue Findings																									
Skeleton																									
Periostitis																									
No Organ Specified																									
Neoplasms																									
Pyemia																									
Soft Tissue																									
Neoplasms																									
Salivary Gland																									
Neoplasms																									
Parathyroid																									
Neoplasms																									

TWO-YEAR TOXICITY STUDY IN RATS

EBI PROJECT #1400

Histological Findings

Group No.	4 - Male - High Dose (Continued)																								
Animal No.	5269	5271	5272	5273	5274	5275	5276	5277[d]	5278	5279	5280	5281	5284[d]	5285[d]	5286	5287[d]	5288[d]	5289	5290	5291	5292[d]	5293	5294	5295[d]	5296
Tissue Findings																									
Pituitary	-	0	-	0	-	-	-	0	0	0	-	0	*	0	0	0	*	-	-	-	0	0	-	0	-
Neoplasms																									
Thyroids	-	0	-	0	-	-	0	0	*	-	*	-	-	0	*	0	-	-	0	*	0	-	-	-	-
Neoplasms																									
C-cell hyperplasia																									
Heart	-	-	-	-		-	-		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Myocardial fibrosis					2																				
Endocardial disease								*																	
Bacterial endocarditis																									
Liver		-	-				-		-	-	-		-		-	-		-	-	-	-	*	-	-	
Neoplasms	*			*																					
Hyalin globules						1						2													3
Fatty change																									
Passive congestion					*									*			*								
Central necrosis								*																	
Reactive foci																									
Spleen	-	-	0	-	-	-	-	-	-	-	-	-	-	-	-			-	-	-	-	-	-	-	-
Increased hemosiderin																	*								
Increased hemopoiesis																*									
Atrophy																									
Reactive hyperplasia																									

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	4 - Male - High Dose (Continued)																										
Animal No.	5269	5271	5272	5273	5274	5275	5276	5277[d]	5278	5279	5280	5281	5284[d]	5285[d]	5286	5287[d]	5288[d]	5289	5290	5291	5292[d]	5293	5294	5295[d]	5296
Tissue Findings																									
Kidneys																									
Chronic inflammation	1	2	5	1	3	1	3		1	3	1	4	3	5	5		4	2		2		4	3		2
Calcinosis																									
Metastatic abscesses																									
Suppurative pyelitis																									
Adrenals			-			-	-	-	-	0	-	-	-	-		-			0	0	0	-	-	-	-
Neoplasms		*			*													1							
Capillary ectasia																	1								
Focal lipidosis	1			2																					
Cortical hemorrhage																									
Focal medullary hyperplasia															+										
Pancreas	-	-		-	-	-	-	0	0	-	-	-	-	-	-	-	-	-	-	-	0	-	-	-	-
Focal acinar atrophy			1																						
Stomach	-	-	-	-	-	-	-		-	-	-	-	-		-	-	-	-	-	-	0	-	-	-	-
Neoplasms								*																	
Mucosal calcification														+											
Small Intestine	-	-	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	-	-	-	-
Large Intestine	-	-	-	0	-	0	0	0	-	0	0	-	0	-		-	-	0	-	0	0	0		-	0
Nematodiasis															+								+		
Mesenteric Lymph Node	-	-	0	0	-	0	-	0	0	0	0	-	-	-	-	0	0	-	-	-	0	-	0	-	-
Lymphadenitis																									

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	4 - Male - High Dose (Continued)																								
Animal No.	5269	5271	5272	5273	5274	5275	5276	5277[d]	5278	5279	5280	5281	5284[d]	5285[d]	5286	5287[d]	5288[d]	5289	5290	5291	5292[d]	5293	5294	5295[d]	5296
Tissue Findings																									
Urinary Bladder	-	-	-	-	-	-	0	0	-	-	-	-	-	0	-	-	-	0	-	-	0	0	-	-	-
Testes	-	-	*	-	-	-		*	-	-	-	-	-	0	-		-	-	-	*	-	-	*		-
Neoplasms																*								*	
Atrophy							+									+								+	
Bone Marrow	-	-	-	0	-	-	0	-	-	-	-	0	-	-	-	-	-	-	-	-	-	-	-	-	0
Granulocytic hyperplasia																									
Decreased cellularity																									
Lung																									
Neoplasms																									
Alveolar histiocytosis																									
Interstitial pneumonia																									
Marine pneumonia						+																			
Integument																									
Neoplasms																									
Abscess																									
Multiple Distribution																									
Polyarteritis															+										
Metastatic calcification														+											
Skeleton																									
Periostitus																									

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	4 - Male - High Dose (Continued)																						
Animal No.	5269	5271	5272	5273	5274	5275	5276	5277[d]	5278	5279	5280	5281	5284[d]	5285[d]	5286	5287[d]	5288[d]	5289	5290	5291	5292[d]	5293	5294	5295[d]	5296
Tissue Findings																									
No Organ Specified																									
Neoplasms																									
Pyemia																									
Soft Tissue																									
Neoplasms																									
Salivary Gland																									
Neoplasms																									
Parathyroid																									
Neoplasms																									

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Females - Control																	
Animal No.	4497	4498	4499	4500	4501	4502	4503	4504	4505	4506[d]	4507[d]	4508	4509[d]	4510	4511	4512	4513	4514[d]
Tissue Findings																		
Pituitary	*	*		*	-	*	-	*	*	-	0	*	*	-	*	0	*	-
Neoplasms																		
Abscess			+															
Thyroids	-	0	-	-	-	0	-	-	-	-	-	-	-	-	-	-	-	-
Neoplasms																		
C-cell hyperplasia																		
Heart	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Myocardial fibrosis							+											
Liver	-	-	-	-	-	-	-	-	-	-		-		-	-	-	-	
Neoplasms													+					
Hyaline globules											3							
Fatty change																		+
Passive congestion																		
Central necrosis																		
Spleen		-	-		0	-		-	-	-		-	-		-	-	-	
Increased hemosiderin	+			+			+							+				+
Increased hemopoiesis											+							
Kidneys						-		-	-	-	-	-	-	-			-	-
Chronic inflammation			4		3		1								2	2		
Calcinosis	1	1	2	1														
Suppurative pyelitis																		

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Females - Control (Continued)																	
Animal No.	4497	4498	4499	4500	4501	4502	4503	4504	4505	4506[d]	4507[d]	4508	4509[d]	4510	4511	4512	4513	4514[d]
Tissue Findings																		
Adrenals									-	-	-		-	-	-		-	
Neoplasms																		
Capillary ectasia	3	2	4	1	3	2		3				3				2		1
Focal lipidosis	3	2					3											
Unilateral necrosis																		
Pancreas	-	-	-	-		-		-	-	-	-		-	-	-	-	-	0
Neoplasms							*											
Focal acinar atrophy					1							1						
Pancreatitis												1						
Stomach	-	-	-	-	-	-	0	-	-	-	-	-	-	-	-	-	-	-
Mucosal calcification																		
Small Intestine	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	-	-	0
Large Intestine	-	-	-	0			-	-	-	-	-	0	-	0	-	-	0	-
Nematodiasis					+	+												
Mesenteric Lymph Node	-	-	-	0	-	0	0	-	0	-	0	0	0	0	-	0	-	0
Lymphectasia																		
Urinary Bladder	-	-	-	-	-	-	-	-	-	0	-	-	-	-	-	-	-	-
Chronic ulcer																		
Ovaries		-	-	-	-	-	-	-		-	-	-	-	-	-	-	-	-
Neoplasms	*																	
Cysts									+									
Bone Marrow	-	0	-	-	-	0	-	-	0	-		-	0	0	-	-	0	-
Erythroid hyperplasia											+							

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Females - Control (Continued)																
Animal No.	4497	4498	4499	4500	4501	4502	4503	4504	4505	4506[d]	4507[d]	4508	4509[d]	4510	4511	4512	4513	4514[d]
Tissue Findings																		
Lung																		
Alveolar histiocytosis																		
Mammary Gland																		
Neoplasms								*		*	*							*
Cystic hyperplasia			*															
Chronic mastitis																		
Uterus																		
Neoplasms																	*	
Hydrometra																		
Multiple Distribution																		
Polyarteritis			*															
Integument																		
Neoplasms	*					*												
No Organ Specified																		
Neoplasms										*								

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Females - Control (Continued)																	
Animal No.	4515	4516[d]	4517[d]	4518	4519	4520[d]	4521	4701	4702	4704	4708	4710	4711	4713	4714	4716	4717[d]	4719
Tissue Findings																		
Pituitary	-	0					-	-	0		-	0	0	0		-	-	-
Neoplasms			*	*	*	*				*					*			
Abscess																		
Thyroids			-			-	-	-	-	-	-	-	-	-	-	0	-	0
Neoplasms																		
C-cell hyperplasia	+	+		+	+													
Heart	-	-	-	-	-	-	-	-	-	-	-	-			-	-	-	-
Myocardial fibrosis													2	2				
Liver	-	-	-		-		-	-	-		-		-	-	-	-	-	-
Neoplasms				*								*						
Hyaline globules						2				3								
Fatty change																		
Passive congestion																		
Central necrosis																		
Spleen	-		-	-	-			-	-		-	-	-	-				
Increased hemosiderin						+	+			+					+	+	+	+
Increased hemopoiesis		+																
Kidneys	-	-				-			-		-				-		-	
Chronic inflammation			1	1	1			2		1		2	1	1		3		3
Calcinosis			2				1			2								
Suppurative pyelitis																		

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Females - Control (Continued)																	
Animal No.	4515	4516	4517[d]	4518[d]	4519	4520	4521[d]	4701	4702	4704	4708	4710	4711	4713	4714	4716	4717	4719[d]
Tissue Findings																		
Adrenals					-					-		-						
Neoplasms						*												
Capillary ectasia	4		4	2			3	2	3		4		4	1	3	2	5	4
Focal lipidosis				2										1				
Unilateral necrosis		+																
Pancreas	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Neoplasms																		
Focal acinar atrophy																		
Pancreatitis																		
Stomach	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Mucosal calcification																		
Small Intestine	-	0	-	-	-	-	-	-	-	-	-	-	-	-	0	-	-	-
Large Intestine	-	-		0	-	-		-	-	0	-	0	-	-	-	-	-	-
Nematodiasis			+				+											
Mesenteric Lymph Node	0	-	-	0	-	-	0	-	-	-	-	0	-	-	-	0	-	0
Lymphectasia																		
Urinary Bladder	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Chronic ulcer																		

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Females - Control (Continued)																	
Animal No.	4515	4516[d]	4517[d]	4518	4519	4520[d]	4521	4701	4702	4704	4708	4710	4711	4713	4714	4716	4717[d]	4719
Tissue Findings																		
Ovaries	-	-	-	-		-	0	-		-	-		-	-	-	-	-	-
Neoplasms																		
Cysts					+				+			+						
Bone Marrow	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Erythroid hyperplasia																		
Lung																		
Alveolar histiocytosis																		
Mammary Gland																		
Neoplasms		*	*	*				*		*								*
Cystic hyperplasia																		
Chronic mastitis																		
Uterus																		
Neoplasms																		
Hydrometra																		
Multiple Distribution																		
Polyarteritis																		
Integument																		
Neoplasms																		
No Organ Specified																		
Neoplasms																		

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Females - Control (Continued)																		
Animal No.	4720	4722[d]	4723[d]	4726	4728	4729[d]	4731	4732	4733	4734	4735	4736	4737[d]	4738[d]	4739[d]	4740	4741	4742[d]
Tissue Findings																		
Pituitary			-	0			-	-		0	-	-	-	-		0	0	-
Neoplasms	*	*			*	*			*						*			
Abscess																		
Thyroids	-	-	0	-		-		-	-		-	-	-	-	-	-	0	-
Neoplasms										*								
C-cell hyperplasia					+		+											
Heart	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Myocardial fibrosis																		
Liver	-	-			-	-	-				-	-	-	-	-	-	-	0
Neoplasms				*				*		*								
Hyaline globules									2									
Fatty change																		
Passive congestion																		
Central necrosis			+															
Spleen		-	-	-	-		-	-	-		-	-			-	-		
Increased hemosiderin						+							+	+			+	
Increased hemopoiesis	+									+								+
Kidneys		-	-		-	-	-	-		-		-	-	-		-		
Chronic inflammation				2							1				2			
Calcinosis									2								1	2
Suppurative pyelitis	2																	

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Females - Control (Continued)																		
Animal No.	4720	4722[d]	4723[d]	4726	4728	4729[d]	4731	4732	4733	4734	4735	4736	4737[d]	4738[d]	4739[d]	4740	4741	4742[d]
Tissue Findings																		
Adrenals	-	-	-	-								-						
Neoplasms																		
Capillary ectasia					4	1	3		4	1	4		3	2	1	1	3	4
Focal lipidosis								3								1	2	2
Unilateral necrosis																		
Pancreas	-	0	-	-	-	-		-	-	-	-	-	-	-	-	-	-	0
Neoplasms																		
Focal acinar atrophy							1											
Pancreatitis																		
Stomach	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Mucosal calcification																		
Small Intestine	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Large Intestine	0	0	-	-	-	-	-	-	-	-	-	-	0	-	0	-	-	-
Nematodiasis																		
Mesenteric Lymph Node	0	0	-	0	-	0	-	0	-	-	-	-	0	-	0	-	0	-
Lymphectasia																		
Urinary Bladder		-	-	-	0	-	0	-	-	-	0	-	-	-	-	-	0	-
Chronic ulcer	+																	
Ovaries		-	0		-	-	-	-	-	-	-		-	-	-	-	-	0
Neoplasms																		
Cysts	+			+								+						

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Females - Control (Continued)																	
Animal No.	4720	4722[d]	4723[d]	4726	4728	4729[d]	4731	4732	4733	4734	4735	4736	4737[d]	4738[d]	4739[d]	4740	4741	4742[d]
Tissue Findings																		
Bone Marrow	-	-		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Erythroid hyperplasia			+															
Lung																		
Alveolar histiocytosis																		
Mammary Gland																		
Neoplasms	*		*	*	*			*	*	*	*							*
Cystic hyperplasia																		
Chronic mastitis																		
Uterus																		
Neoplasms																		
Hydrometra																		
Multiple Distribution																		
Polyarteritis																		
Integument																		
Neoplasms																*		
No Organ Specified																		
Neoplasms		*			*								*	*				

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Females - Control (Continued)																		
Animal No.	4743	4744[d]	4745	4746	4747	4748	4749	4750	4757[d]	4758	4760	4761	4764	4765	4767[d]	4769[d]	4770	4771
Tissue Findings																		
Pituitary	-					-	-			-	-		-				-	
Neoplasms		*	*	*	*			*	*			*		*	*	*		*
Abscess																		
Thyroids	-	-	-	-	-	-		-	-	-	-	-	-	-		-	-	-
Neoplasms																		
C-cell hyperplasia							+								+			
Heart	-	-	-	-	-	-	-	-	-	-	-	-	-	-			-	-
Myocardial fibrosis															1	1		
Liver		-	-	-		-	-	-	-	-	-		-	-	-			
Neoplasms																		*
Hyaline globules	1				3							1					1	
Fatty change																3		
Passive congestion																		
Central necrosis																		
Spleen	-		-	-	-	-	0		-		-		-	0			-	-
Increased hemosiderin		+						+				+			+	+		
Increased hemopoiesis										+								
Kidneys				-				-		-		-	-	-				
Chronic inflammation		3	2			1	1											
Calcinosis	3				2				3		1				2	1	1	2
Suppurative pyelitis																		

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Females - Control (Continued)																		
Animal No.	4743	4744[d]	4745	4746	4747	4748	4749	4750	4757[d]	4758	4760	4761	4764	4765	4767[d]	4769[d]	4770	4771
Tissue Findings																		
Adrenals		-	-								-					-		
Neoplasms																		
Capillary ectasia	1			3			2	3	3	3		3	3	3	3		5	3
Focal lipidosis					2	3						2			1			
Unilateral necrosis																		
Pancreas	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Neoplasms																		
Focal acinar atrophy																		
Pancreatitis																		
Stomach	-	-	-	-	-	-	-	-	-	-	0	-	-	-	-		-	-
Mucosal calcification																+		
Small Intestine	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Large Intestine	-	-	-	-	-	0	-	-	-	-	0	-	0	0	-	-	-	-
Nematodiasis																		
Mesenteric Lymph Node	0	-	0	0	-	-	-	0	-	-	0	-		-	-	-	0	-
Lymphectasia													+					
Urinary Bladder	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Chronic ulcer																		
Ovaries	-	-	-	-	-	-	-	-	-		-	-	-	-	-	-	-	-
Neoplasms																		
Cysts										+								

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Females - Control (Continued)																
Animal No.	4743	4744[d]	4745	4746	4747	4748	4749	4750	4757[d]	4758	4760	4761	4764	4765	4767[d]	4769[d]	4770	4771
Tissue Findings																		
Bone Marrow	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Erythroid hyperplasia																		
Lung																		
Alveolar histiocytosis								+										
Mammary Gland																		
Neoplasms			*	*	*	*										*		
Cystic hyperplasia																		
Chronic mastitis		+																
Uterus																		
Neoplasms																		
Hydrometra		+																
Multiple Distribution																		
Polyarteritis																		
Integument																		
Neoplasms																		
No Organ Specified																		
Neoplasms		*																

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	4 - Female - High Dose																			
Animal No.	4647	4648	4649[d]	4650	4651	4652	4653	4654	4655	4656[d]	4657	4658	4660[d]	4661[d]	4662[d]	4663	4664	4665[d]	4667[d]	4668[d]
Tissue Findings																				
Pituitary	*	0	*	*	0	*	0	*	*	*	*	*	*	*	*	*	0	-	-	*
Neoplasms																				
Cyst																				
Thyroids	-	-	-	-	-	0	-	-	-	-	-	-	-	-	-	0	0	-	0	-
Neoplasms																				
C-cell hyperplasia																				
Heart	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2
Myocardial fibrosis																				
Liver	-	-	-	-	-	-	-	-	-	-		0		-	-	-	-	-	-	
Neoplasms													2							
Hyaline globules																				*
Fatty change																				
Passive congestion																				
Central necrosis																				
Bile duct proliferation																				
Increased hemosiderin											*									
Infarction																				
Congenital cyst																				
Spleen	*	*	*	-	*		-	*	-		-	-	-	-	*	-	-	*	-	*
Increased hemosiderin						*														
Increased hemopoiesis										*	*									
Increased granulopoiesis																				

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	4 - Female - High Dose (Continued)																			
Animal No.	4647	4648	4649[d]	4650	4651	4652	4653	4654	4655	4656[d]	4657	4658	4660[d]	4661[d]	4662[d]	4663	4664	4665[d]	4667[d]	4668[d]
Tissue Findings																				
Kidneys	-		-	-	-		-		-		-		-			-		-		
Chronic inflammation							2				4		2	1		2		1		1
Calcinosis	3		1			4		1		4					2			2		2
Suppurative pyelitis																				
Interstitial nephritis																				
Congenital cyst																				
Adrenals		-	-	-			-		-			-								
Capillary ectasia	1				4	4		3					3	3	3	4	4	1	3	3
Focal lipidosis										3	3		1							
Pancreas	-	-	0	-	-	-	-	-	-	-	-	-	-	-	-		-	-	0	-
Focal acinar atrophy																2				
Stomach	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Neoplasms																				
Chronic inflammation																				
Small Intestine	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	0	0
Large Intestine	-	-	-	-	-	-	-		-	-	0	-	-	-	-	0	-	-	0	
Nematodiasis								+												
Chronic colitis																				+
Mesenteric Lymph Node			0	-	0	-	0	-	-	0	0	-	0	-	0	-	0	-	0	
Reactive hyperplasia																				+
Increased pigmentation	+	-																		

TWO-YEAR TOXICITY STUDY IN RATS

LRI PROJECT #1400

Histological Findings

Group No.	4 - Female - High Dose (Continued)																			
Animal No.	4647	4648	4649[d]	4650	4651	4652	4653	4654	4655	4656[d]	4657	4658	4660[d]	4661[d]	4662[d]	4663	4664	4665[d]	4667[d]	4668[d]
Tissue Findings																				
Urinary Bladder	-	-	-	-	-	-	-	0	-	-	-	-	-	-	-	-	-	-	-	-
Cystitis																		3		
Urolith																				
Ovaries		-	-	-		-	-	-	-	-	-	0	-	-	-	-		-	-	-
Cyst/s	+				+															
Bone Marrow	-	-	-	-	-	-	-	-	-		-	-	-	-		-		-	-	-
Erythroid hyperplasia										+										
Granulocytic hyperplasia															+		+			
Decreased cellularity																				
Lung												2								
Alveolar histiocytosis															2					
Bronchopneumonia																				
Abscess																				
Mammary Gland				+				+		+	+						+	+	+	
Neoplasms														+	+	+				
Galactocele																				
Uterus										+										
Neoplasm				+																
Endometrial polyp								•												

TWO-YEAR TOXICITY STUDY IN RATS

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Histological Findings

Group No.	4 - Female - High Dose (Continued)
Animal No.	4647 4648 4649[d] 4650 4651 4652 4653 4654 4655 4656[d] 4657 4658 4660[d] 4661[d] 4662[d] 4663 4664 4665[d] 4667[d] 4668[d]
Tissue Findings	
Thymus	
Neoplasms	
No Organ Specified	
Neoplasms	
Chronic abscess	
Acute peritonitis	
Chronic peritonitis	
Fat necrosis	
Integument	
Neoplasms	
Soft Tissue	
Neoplasms	

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	4 - Female - High Dose (Continued)																				
Animal No.	4669[d]	4670	4671[d]	5147	5148	5149[d]	5151	5152	5154[d]	5155	5158	5160	5163[d]	5164	5166	5167	5169[d]	5170	5172	5173[d]
Tissue Findings																				
Pituitary	-	-		-		0	•	0			0	-		-		0	0	-		-
Neoplasms					*		*		*	*			*		*				*	
Cyst			+																	
Thyroids	-	-	-	-	-	0	-	-	0			-	-	-	-	-	-	-	-	-
Neoplasms										*										
C-cell hyperplasia											+									
Heart	-	-	-	-	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Myocardial fibrosis																				
Liver	-	-		-		-		-	-	-	-	-		-	-	-		-	-	-
Neoplasms					*															
Hyaline globules																				
Fatty change																	3			
Passive congestion																				
Central necrosis													+				+			
Bile duct proliferation							2													
Increased hemosiderin			+																	
Infarction																				
Congenital cyst																				
Spleen	-	-		-					-	-	-	-	-	0		-			-	
Increased hemosiderin			+			+	+	+							+			+		
Increased hemopoiesis					+												+			+
Increased granulopoiesis																				

TWO-YEAR TOXICITY STUDY IN RATS

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Histological Findings

Group No.	4 - Female - High Dose (Continued)																			
Animal No.	4669[d]	4670	4671[d]	5147	5148	5149[d]	5151	5152	5154[d]	5155	5158	5160	5163[d]	5164	5166	5167	5169[d]	5170	5172	5173[d]
Tissue Findings																				
Kidneys	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Chronic inflammation		1										1			1					
Calcinosis	1				2			4							2			2	2	
Suppurative pyelitis					3			3												
Interstitial nephritis																				
Congenital cyst																			+	
Adrenals	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Capillary ectasia	1	3	2		2	2	4	2					5				1		5	
Focal lipidosis																				
Pancreas	0	-	-	-	-	-	-		0	-	-	-	0	-	-	-	-	-	-	-
Focal acinar atrophy		1						2												
Stomach	-	-		-	-	-	-	-	-	-	0	-	-	0	-	-	-	-	-	-
Neoplasms																				
Chronic inflammation			+																	
Small Intestine	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Large Intestine	-	0	-	0	-	-	-	0	-	0	0	-	-	-	-	-	0	-	0	-
Nematodiasis																				
Chronic colitis																				
Mesenteric Lymph Node	0	-	-	0	0	-	-	-	0	0	-	-	-	-	-	-	-	0	0	-
Reactive hyperplasia																				
Increased pigmentation																				
Urinary Bladder	-	-	-	-		-	-		-	-	0	-	-	-	-	-	0	-	-	-
Cystitis								3												
Urolith					+			+												

TWO-YEAR TOXICITY STUDY IN RATS

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Histological Findings

Group No.	4 - Female - High Dose (Continued)																				
Animal No.	4669[d]	4670	4671[d]	5147	5148	5149[d]	5151	5152	5154[d]	5155	5158	5160	5163[d]	5164	5166	5167	5169[d]	5170	5172	5173[d]
Tissue Findings																				
Ovaries	-		-	-	-	-	-		-	-	-		-		-	-	-	-	-	-
Cyst/s		+						+				+		+						
Bone Marrow	0	0	-	0	-	-	-	0	-	-	0	-	-	-	-	-	-	-	-	
Erythroid hyperplasia																				
Granulocytic hyperplasia																				+
Decreased cellularity																				
Lung																				
Alveolar histiocytosis							2							2						
Bronchopneumonia																				
Abscess																				
Mammary Gland																				
Neoplasms										*			*		*				*	
Galactocele																				
Uterus																				
Neoplasms																				+
Endometrial polyp																				
Thymus																				
Neoplasms											*									
No Organ Specified																				
Neoplasms																	*			
Chronic abscess					+											+				
Acute peritonitis																				+
Chronic peritonitis																				
Fat necrosis																				

TWO-YEAR TOXICITY STUDY IN RATS

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Histological Findings

Group No.	4 - Female - High Dose (Continued)
Animal No.	4669[d] 4670 4671[d] 5147 5148 5149[d] 5151 5152 5154[d] 5155 5158 5160 5163[d] 5164 5166 5167 5169[d] 5170 5172 5173[d]
Tissue Findings	
Integument	
Neoplasms	
Soft Tissue	
Neoplasms	

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Histological Findings

Group No.	4 - Female - High Dose (Continued)																				
Animal No.	5175	5176	5178[d]	5179	5181	5182	5183[d]	5185	5189	5190[d]	5191	5192[d]	5193[d]	5194	5195	5196	5197	5198[d]	5199	5200
Tissue Findings																				
Pituitary	-		-			0	-	0	0	0				-	-		-	-		-
Neoplasms		*		*	*						*	*	*			*			*	
Cyst																				
Thyroids	-	-	-	-	-	-	-	-	0	-	-	-	-	-		-	0	-	-	-
Neoplasms															*					
C-cell hyperplasia																				
Heart	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Myocardial fibrosis																				
Liver	-		-	-	-	-		-	-		-		-	-	-	-	-			-
Neoplasms										*									*	
Hyaline globules												1								
Fatty change																		4		
Passive congestion																				
Central necrosis							+													
Bile duct proliferation																				
Increased hemosiderin																				
Infarction																				
Congenital cyst		+																		
Spleen	-			-		-		-		-				-		-	-	-	-	
Increased hemosiderin					+		+		+		+	+	+		+					+
Increased hemopoiesis		+	+									●								
Increased granulopoiesis																				

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	4 - Female - High Dose (Continued)																				
Animal No.	5175	5176	5178[d]	5179	5181	5182	5183[d]	5185	5189	5190[d]	5191	5192[d]	5193[d]	5194	5195	5196	5197	5198[d]	5199	5200
Tissue Findings																				
Kidneys	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Chronic inflammation		1		2				1								2				1
Calcinosis	1											3					1			
Suppurative pyelitis																				
Interstitial nephritis																		3		
Congenital cyst									+											
Adrenals										-			-					0		
Capillary ectasia		3	1	3	2		2	1	3		4	2		2	2	3	2		4	
Focal lipidosis	2	2			2	3								2						2
Pancreas	-	-	-	-	-	-	-	-	-	0	-	-	-	-	-	-	-	0	-	-
Focal acinar atrophy																				
Stomach	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Neoplasms																				
Chronic inflammation																				
Small Intestine	-	-	-	-	-	-	-	-	-	0	-	-	-	-	-	-	-	0	-	-
Large Intestine	0	-	-	-	-	0	-	-	-	-	-	-	0	-	-	0	-	0	-	0
Nematodiasis																				
Chronic colitis																				
Mesenteric Lymph Node	0	0	-	0	-	0	-	-	0	0	-	-	-	0	-	-	-	0	-	-
Reactive hyperplasia																				
Increased pigmentation																				

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	4 - Female - High Dose (Continued)																				
Animal No.	5175	5176	5178[d]	5179	5181	5182	5183[d]	5185	5189	5190[d]	5191	5192[d]	5193[d]	5194	5195	5196	5197	5198[d]	5199	5200
Tissue Findings																				
Urinary Bladder	-	0	-	-	-	0	-	-	-	0	-	-	-	-	-	-	-	0	0	-
Cystitis																				
Urolith																				
Ovaries	-	-	-	-	-	-	-	-	-	0	-		0	-	-	-	-	0	-	-
Cyst/s												+								
Bone Marrow	0	0	-	-	-	-		-	-	-	-	-	-	-	-	-	-	-	-	0
Erythroid hyperplasia							+													
Granulocytic hyperplasia																				
Decreased cellularity																				
Lung																				
Alveolar histiocytosis																				
Bronchopneumonia																				
Abscess																				
Mammary Gland																				
Neoplasms						*	*	*		*				*			*		*	
Galactocele																				
Uterus																				
Neoplasms		*																		
Endometrial polyp				+																
Thymus																				
Neoplasms																				

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	4 - Female - High Dose (Continued)
Animal No.	5175 5176 5178[d] 5179 5181 5182 5183[d] 5185 5189 5190[d] 5191 5192[d] 5193[d] 5194 5195 5196 5197 5198[d] 5199 5200
Tissue Findings	
No Organ Specified	
Neoplasms	
Chronic abscess	
Acute peritonitis	
Chronic peritonitis	
Fat necrosis	
Integument	
Neoplasms	
Soft Tissue	
Neoplasms	

TWO-YEAR TOXICITY STUDY IN RATS

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Histological Findings

Group No.	4 - Female - High Dose (Continued)																				
Animal No.	5201[d]	5202	5203[d]	5204[d]	5205	5206	5207	5208	5209	5210[d]	5211	5212[d]	5213	5214	5215	5217	5218[d]	5219	5220	5221	
Tissue Findings																					
Pituitary	-		-	-		-			-	0		-	0	-	0		-			-	
Neoplasms		*			*		*	*			*					*		*	*		
Cyst																					
Thyroids	-		0	0	-			-	-	0	-	0			0	0	-	-	-	-	
Neoplasms						*							*								
C-cell hyperplasia		+					+							+							
Heart	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Myocardial fibrosis																					
Liver				-	-	-	-		-	-	-		-	-		-	-			-	
Neoplasms		*													*						
Hyaline globules																		3	2		
Fatty change																					
Passive congestion	+																				
Central necrosis			+									+									
Bile duct proliferation																					
Increased hemosiderin								+													
Infarction																					
Congenital cyst																					
Spleen				-		-	-		-		-	-	-	-	-			-	-	-	
Increased hemosiderin	+	+			+			+									+				
Increased hemopoiesis			+					+								+					
Increased granulopoiesis										+											

TWO-YEAR TOXICITY STUDY IN RATS

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Histological Findings

Group No.	4 - Female - High Dose (Continued)																			
Animal No.	5201[d]	5202	5203[d]	5204[d]	5205	5206	5207	5208	5209	5210[d]	5211	5212[d]	5213	5214	5215	5217	5218[d]	5219	5220	5221
Tissue Findings																				
Kidneys	-	-	-	-			-		-			-	-		-				-	-
Chronic inflammation						2		1			1			2						
Calcinosis					2					3						2	1	2		
Suppurative pyelitis																				
Interstitial nephritis																				
Congenital cyst																				
Adrenals	-							-							0		-			
Capillary ectasia		2	5				2		2	3	3	3	4	2		1		4	3	3
Focal lipidosis				1	2	2			2					1				3	1	
Pancreas	-	-	-	0	-	-	-	-	-	-	-	0	-	-	-	-	-	-	-	-
Focal acinar atrophy																				
Stomach		-	-	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Neoplasms	•																			
Chronic inflammation																				
Small Intestine	-	-	-	0	-	-	-	-	0	0	-	0	-	-	-	-	-	-	-	-
Large Intestine	-	0	-	-	-	0	-	-	0	0	-	0	0	0	-	-	-	0	-	0
Nematodiasis																				
Chronic colitis																				
Mesenteric Lymph Node	0	-	-	0	0	-	-	0	0	0	-	0	0	0	0	0	0	-	-	-
Reactive hyperplasia																				
Increased pigmentation																				

TWO-YEAR TOXICITY STUDY IN RATS

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Histological Findings

Group No	4 - Female - High Dose (Continued)																			
Animal No.	5201[d]	5202	5203[d]	5204[d]	5205	5206	5207	5208	5209	5210[d]	5211	5212[d]	5213	5214	5215	5217	5218[d]	5219	5220	5221
Tissue Findings																				
Urinary Bladder	-	-	-	-	-	-	-	-	-	0	-	0	-	-	-	-	-	-	-	-
Cystitis																				
Urolith																				
Ovaries	-	-	0	0	-	-	-	0	-	0	-	0		-	-				-	-
Cyst/s													+			+	+	+		
Bone Marrow		-	-	-	0	-	0	-	0		-	-	-	0	-	-	-	0	-	-
Erythroid hyperplasia																				
Granulocytic hyperplasia	+									+										
Decreased cellularity																				
Lung																				
Alveolar histiocytosis		2																		2
Bronchopneumonia																				
Abscess										+										
Mammary Gland			*	*	*	*	*	*			*	*	*			*		*	*	*
Neoplasms																				
Galactocele																				
Uterus																				
Neoplasms																				
Endometrial polyp																				
Thymus																				
Neoplasms																				

TWO-YEAR TOXICITY STUDY IN RATS

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Histological Findings

Group No.	4 - Female - High Dose (Continued)																		
Animal No.	5201[d]	5202	5203[d]	5204[d]	5205	5206	5207	5208	5209	5210[d]	5211	5212[d]	5213	5214	5215	5217	5218[d]	5219	5220	5221
Tissue Findings																				
No Organ Specified																				
Neoplasms																				
Chronic abscess																				
Acute peritonitis																				
Chronic peritonitis																				
Fat necrosis																				
Integument																				
Neoplasms																				
Soft Tissue																				
Neoplasms																				

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No.	1 - Male - Control																		
Animal No.	4522	4523	4525	4526	4527	4528[a]	4529	4530	4531	4532[d]	4534[d]	4535	4537	4538	4539	4540	4541[d]	4542	4543	4544
Tissue Findings																				
Pituitary																				
Adenoma						+									+	+				
Thyroids																				
C-cell adenoma																				
Liver - Preneoplastic Alterations																				
Basophilic focus			+																	
Eosinophilic focus				+																
Clear cell focus																				
Liver - Neoplasms																				
Hepatocellular carcinoma																				
Adrenals																				
Cortical adenoma																				
Pheochromocytoma																				
Cortical carcinoma																				
Pancreas																				
Islet cell adenoma																				
Testes																				
Interstitial cell tumor														+						
Mammary Gland																				
Adenocarcinoma																+				
Lung																				
Alveolar bronchiolar adenoma									+											

TWO-YEAR TOXICITY STUDY IN RATS

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NEOPLASMS

Group No.	1 - Male - Control (Continued)																		
Animal No.	4522	4523	4525	4526	4527	4528[d]	4529	4530	4531	4532[d]	4534[d]	4535	4537	4538	4539	4540	4541[d]	4542	4543	4544
Tissue Findings																				
No Organ Specified																				
Multiple plasmacytoma																				
Myeloid leukemia																				
Carcinoma																				
Adenocarcinoma																				
Synovial sarcoma																				
Soft Tissue																				
Fibroma																				
Integument																				
Squamous cell carcinoma																				
Parathyroid																				
Adenoma																				

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No.	1 - Male - Control (Continued)																		
Animal No.	4545	4546	4773	4774[d]	4776[d]	4777	4778[d]	4780	4782	4783[d]	4785	4786	4788	4791[d]	4792	4794	4795[d]	4797[d]	4798[d]	4800
Tissue Findings																				
Pituitary																				
Adenoma							+					+				+		+	+	
Thyroids																				
C-cell adenoma															+					
Liver - Preneoplastic Alterations																				
Basophilic focus																				
Eosinophilic focus																				
Clear cell focus						+														
Liver - Neoplasms																				
Hepatocellular carcinoma																				
Adrenals																				
Cortical adenoma		+																		
Pheochromocytoma																				
Cortical carcinoma																				
Pancreas																				
Islet cell adenoma									+	+										
Testes																				
Interstitial cell tumor									+											
Mammary Gland																				
Adenocarcinoma																				

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No.	1 - Male - Control (Continued)
Animal No.	4545 4546 4773 4774[d] 4776[d] 4777 4778[d] 4780 4782 4783[d] 4785 4786 4788 4791[d] 4792 4794 4795[d] 4797[d] 4798[d] 4800
Tissue Findings	
Lung	
Alveolar bronchiolar adenoma	+
No Organ Specified	
Multiple plasmacytoma	+
Myeloid leukemia	
Carcinoma	+
Adenocarcinoma	
Synovial sarcoma	
Soft Tissue	
Fibroma	+
Integument	
Squamous cell carcinoma	
Parathyroid	
Adenoma	+

TWO-YEAR TOXICITY STUDY IN RATS

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NEOPLASMS

Group No.	1 - Male - Control (Continued)																	
Animal No.	4825[d]	4826[d]	4827[d]	4828	4829[d]	4830	4831	4832[d]	4833	4834	4835	4836[d]	4837	4839	4841[d]	4842	4843[d]	4844	4846
Tissue Findings																			
Pituitary																			
Adenoma		+								+									
Thyroids																			
C-cell adenoma																			
Liver - Preneoplastic Alterations																			
Basophilic focus																			
Eosinophilic focus																			
Clear cell focus																			
Liver - Neoplasms																			
Hepatocellular carcinoma																			
Adrenals																			
Cortical adenoma																			
Pheochromocytoma				+		+													
Cortical carcinoma		+																	
Pancreas																			
Islet cell adenoma																			
Testes																			
Interstitial cell tumor										+									
Mammary Gland																			
Adenocarcinoma																			

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No.	1 - Male - Control (Continued)																	
Animal No.	4825[d]	4826[d]	4827[d]	4828	4829[d]	4830	4831	4832[d]	4833	4834	4835	4836[d]	4837	4839	4841[d]	4842	4843[d]	4844	4846
Tissue Findings																			
Lung																			
Alveolar bronchiolar adenoma																			
No Organ Specified																			
Multiple plasmacytoma																			
Myeloid leukemia	+																		
Carcinoma																			
Adenocarcinoma														+					
Synovial sarcoma															+				
Soft Tissue																			
Fibroma									+										
Integument																			
Squamous cell carcinoma		+																	
Parathyroid																			
Adenoma																	+		

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No.	1 - Male - Control (Continued)																	
Animal No.	4801	4803[d]	4804	4806	4807	4808[d]	4809	4810	4811	4814	4815[d]	4817	4818[d]	4819[d]	4820[d]	4821	4822	4823[d]	4824[d]
Tissue Findings																			
Pituitary																			
Adenoma	+					+		+	+		+		+	+				+	+
Thyroids																			
C-cell adenoma																			
Liver - Preneoplastic Alterations																			
Basophilic focus																			
Eosinophilic focus																			
Clear cell focus																			
Liver - Neoplasms																			
Hepatocellular carcinoma								+											
Adrenals																			
Cortical adenoma																			
Pheochromocytoma										+									
Cortical carcinoma																			
Pancreas																			
Islet cell adenoma																			
Testes																			
Interstitial cell tumor				+		+													
Mammary Gland																			
Adenocarcinoma																			

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No.	1 - Male - Control (Continued)
Animal No.	4801 4803[d] 4804 4806 4807 4808[d] 4809 4810 4811 4814 4815[d] 4817 4818[d] 4819[d] 4820[d] 4821 4822 4823[d] 4824[d]
Tissue Findings	
Lung	
Alveolar bronchiolar adenoma	
No Organ Specified	
Multiple plasmacytoma	
Myeloid leukemia	
Carcinoma	
Adenocarcinoma	
Synovial sarcoma	
Soft Tissue	
Fibroma	
Integument	
Squamous cell carcinoma	
Parathyroid	
Adenoma	

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No.	4 - Male - High Dose																							
Animal No.	4672	4673[d]	4674	4675	4677	4678	4680	4681	4682	4683[d]	4684	4685[d]	4686	4687[d]	4688[d]	4689	4690[d]	4691	4692	4693[d]	4694[d]	4695	4696[d]	5223[d]	5226
Tissue Findings																									
Pituitary																									
Adenoma			+										+												
Thyroids																									
C-cell adenoma																									
Liver - Preneoplastic Alterations																									
Clear cell focus				+																					
Liver - Neoplasms																									
Neoplastic nodules																						+			
Hepatocellular carcinoma																									
Adrenals																									
Pheochromocytoma		+																							
Stomach																									
Squamous papilloma																									
Testes																									
Interstitial cell tumor									+			+													
Salivary Gland																									
Mixed tumor																									
Lung																									
Alveolar bronchiolar adenoma																									

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No.	4 - Male - High Dose																							
Animal No.	4672	4673[d]	4674	4675	4677	4678	4680	4681	4682	4683[d]	4684	4685[d]	4686	4687[d]	4688[d]	4689	4690[d]	4691	4692	4693[d]	4694[d]	4695	4696[d]	5223[d]	5226
Tissue Findings																									
No Organ Specified																									
Sarcoma																									
Lymphosarcoma																									
Carcinoma																									
Soft tissue																									
Fibroma																									
Integument																									
Squamous cell carcinoma																									
Parathyroid																									
Adenoma																									

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No.	4 - Male - High Dose (Continued)																						
Animal No.	5227	5229[d]	5230	5232	5233	5235[d]	5236	5237[d]	5238	5239	5246[d]	5249[d]	5250[d]	5251[d]	5253	5254	5255	5259	5260	5261	5262	5263	5265[d]	5266[d]	5268[d]
Tissue Findings																									
Pituitary																									
Adenoma		+																	+		+				+
Thyroids																									
C-cell adenoma		+																							
Liver - Preneoplastic Alterations																									
Clear cell focus																									
Liver - Neoplasms																									
Neoplastic nodules																									
Hepatocellular carcinoma																									
Adrenals																									
Pheochromocytoma			+																	+					
Stomach																									
Squamous papilloma																									
Testes																									
Interstitial cell																									
tumor			+			+	+																		
Salivary gland																									
Mixed tumor																									

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No.	4 - Male - High Dose (Continued)																							
Animal No.	5227	5229[d]	5230	5232	5233	5235[d]	5236	5237[d]	5238	5239	5246[d]	5249	5250[d]	5251[d]	5253	5254	5255	5259	5260	5261	5262	5263	5265[d]	5266[d]	5268[d]
Tissue Findings																									
Lung																									
Alveolar bronchiolar adenoma																					+				
No Organ Specified																									
Sarcoma		+									+														
Lymphosarcoma																									+
Carcinoma								+																	
Soft Tissue																									
Fibroma												+													+
Integument																									
Squamous cell carcinoma												+													
Parathyroid																									
Adenoma																									

[illegible]-YEAR TOXICITY STUDY IN RATS

[illegible] PROJECT #[illegible]

NEOPLASMS

Group No.	4 - Male - High Dose (Continued)
Animal No.	5269 5271 5272 5273 5274 5275 5276 5277[A] 5278 5279 5280 5281 5284[A] 5285 5286 5287 5288[A] 5289 5290 5291 5292[A] 5293 5294 5295[A] 5296
Tissue Findings	
Pituitary	
Adenoma	• •
Thyroids	
C-cell adenoma	• • • •
Liver - Preneoplastic Alterations	
Clear cell focus	
Liver - Neoplasms	
Basophilic nodules	• •
Hepatocellular carcinoma	•
Adrenals	
Pheochromocytoma	• •
Stomach	
Squamous papilloma	•
Testes	
Interst. tal cell tumor	• • • •
Salivary Gland	
Mixed tumor	•
Lung	
Alveolar bronchiolar adenoma	

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No.	4 - Male - High Dose (Continued)																					
Animal No.	5269	5271	5272	5273	5274	5275	5276	5277[d]	5278	5279	5280	5281	5284[d]	5285	5286	5287	5288[d]	5289	5290	5291	5292[d]	5293	5294	5295[d]	5296
Tissue Findings																									
No Organ Specified																									
Sarcoma																									
Lymphosarcoma																									
Carcinoma																									
Soft Tissue																									
Fibroma																									
Integument																									
Squamous cell carcinoma																									
Parathyroid																									
Adenoma																									

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No.	Females - Control																
Animal No.	4497	4498	4499	4500	4501	4502	4503	4504	4505	4506[d]	4507[d]	4508	4509[d]	4510	4511	4512	4513	4514[d]
Tissue Findings																		
Pituitary																		
Adenoma	+	+		+		+		+	+			+	+		+		+	
Thyroids																		
C-cell adenoma																		
Liver - Preneoplastic Alterations																		
Clear cell focus																		
Basophilic focus													+					
Liver - Neoplasms																		
Neoplastic nodule																		
Hepatocellular carcinoma																		
Adrenals																		
Cortical adenoma																		
Pancreas																		
Islet cell adenoma							+											
Ovaries																		
Sarcoma	+																	
Integument																		
Basal cell carcinoma	+																	
Fibrosarcoma																		
Mammary Gland																		
Fibroadenoma								+		+								+
Adenocarcinoma											+							

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No.	Females - Control (Continued)																
Animal No.	4497	4498	4499	4500	4501	4502	4503	4504	4505	4506[d]	4507[d]	4508	4509[d]	4510	4511	4512	4513	4514[d]
Tissue Findings																		
Uterus																		
Leiomyoma																		
No Organ Specified																		
Sarcoma																		
Lymphosarcoma																		
Reticulum cell sarcoma																		
Malignant lymphoma																		
Myeloid leukemia																		

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No.	Females - Control (Continued)															
Animal No.	4515	4516[d]	4517[d]	4518	4519	4520[d]	4521	4701	4702	4704	4708	4710	4711	4713	4714	4716	4717[d]	4719
Tissue Findings																		
Pituitary																		
Adenoma	+		+	+	+	+				+					+			
Thyroids																		
C-cell adenoma																		
Liver - Preneoplastic Alterations																		
Clear cell focus												+						
Basophilic focus				+								+						
Liver - Neoplasms																		
Neoplastic nodule																		
Hepatocullular carcinoma																		
Adrenals																		
Cortical adenoma						+												
Pancreas																		
Islet cell adenoma																		
Ovaries																		
Sarcoma																		
Integument																		
Basal cell carcinoma																		
Fibrosarcoma																		

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No.	Females - Control (Continued)																
Animal No.	4515	4516[d]	4517[d]	4518	4519	4520[d]	4521	4701	4702	4704	4708	4710	4711	4713	4714	4716	4717[d]	4719
Tissue Findings																		
Mammary Gland																		
Fibroadenoma	+	+	+				+											+
Adenocarcinoma	+									+								
Uterus																		
Leiomyoma																		
No Organ Specified																		
Sarcoma																		
Lymphosarcoma																		
Reticulum cell sarcoma																		
Malignant lymphoma																		
Myeloid leukemia																		

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No.	Females - Control (Continued)																
Animal No.	4720	4722[d]	4723[d]	4726	4728	4729	4731	4732	4733	4734	4735	4736	4737[d]	4738[d]	4739[d]	4740	4741	4742[d]
Tissue Findings																		
Pituitary																		
Adenoma	+	+			+	+			+						+			
Thyroids																		
C-cell adenoma										+								
Liver - Preneoplastic Alterations																		
Clear cell focus																		
Basophilic focus								+										
Liver - Neoplasms																		
Neoplastic nodule																		
Hepatocellular carcinoma				+						+								
Adrenals																		
Cortical adenoma																		
Pancreas																		
Islet cell adenoma																		
Ovaries																		
Sarcoma																		
Integument																		
Basal cell carcinoma																		
Fibrosarcoma																+		
Mammary Gland																		
Fibroadenoma	+		+	+	+			+	+	+	+							+
Adenocarcinoma											+							

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No.	Females - Control (Continued)																	
Animal No.	4720	4722[d]	4723[d]	4726	4728	4729	4731	4732	4733	4734	4735	4736	4737[d]	4738[d]	4739[d]	4740	4741	4742[d]
Tissue Findings																		
Uterus																		
Leiomyoma																		
No Organ Specified																		
Sarcoma																		
Lymphosarcoma																		
Reticulum cell sarcoma																		
Malignant lymphoma																		
Myeloid leukemia																		

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No.	Females - Control (Continued)																
Animal No.	4743	4744[d]	4745	4746	4747	4748	4749	4750	4757[d]	4758	4760	4761	4764	4765	4767[d]	4769[d]	4770	4771
Tissue Findings																		
Pituitary																		
Adenoma	+	+	+	+			+	+				+		+	+	+		+
Thyroids																		
C-cell adenoma																		
Liver - Preneoplastic Alterations																		
Clear cell focus																		
Basophilic focus																		+
Liver - Neoplasms																		
Neoplastic nodule																		
Hepatocellular carcinoma																		
Adrenals																		
Cortical adenoma																		
Pancreas																		
Islet cell adenoma																		
Ovaries																		
Sarcoma																		
Integument																		
Basal cell carcinoma																		
Fibrosarcoma																		
Mammary Gland																		
Fibroadenoma					+		+									+		
Adenocarcinoma			+			+												

TWO-YEAR TOXICITY STUDY IN RATS

L81 PROJECT #1400

NEOPLASMS

Group No.	Females - Control (Continued)
Animal No.	4743 4744[d] 4745 4746 4747 4748 4749 4750 4757[d] 4758 4760 4761 4764 4765 4767[d] 4769[d] 4770 4771
Tissue Findings	
Uterus	
Leiomyoma	
No organ specified	
Sarcoma	
Lymphosarcoma	
Reticulum cell sarcoma	
Malignant lymphoma	
Myeloid leukemia	

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No.	4 - Female - High Dose																			
Animal No.	4647	4648	4649[d]	4650	4651	4652	4653	4654	4655	4656[d]	4657	4658	4660[d]	4661	4662[d]	4663	4664[d]	4665[d]	4667[d]	4668[d]	4669
Tissue Findings																					
Pituitary																					
Adenoma	+		+	+		+		+	+	+	+	+	+	+	+	+			+		
Thyroids																					
C-cell adenoma																					
Thymus																					
Thymoma																					
Liver - Preneoplastic Alterations																					
Basophilic focus																					
Liver - Neoplasms																					
Neoplastic nodule																					
Carcinoma																					
Stomach																					
Squamous cell carcinoma																					
Integument																					
Fibroma																					
Squamous cell carcinoma																					+
Uterus																					
Leiomyosarcoma										+											
Adenocarcinoma																					
Carcinoma																					

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No.	4 - Female - High Dose (Continued)																			
Animal No.	4647	4648	4649[d]	4650	4651	4652	4653	4654	5655	4656[d]	4657	4658	4660[d]	4661	4662[d]	4663	4664[d]	4665[d]	4667[d]	4668[d]	4669
Tissue Findings																					
Mammary Gland																					
Adenoma																			+		
Fibroadenoma				+				+			+					+					
Adenocarcinoma										+	+							+			
No Organ Specified																					
Sarcoma			+																		
Myelosarcoma																					
Malignant lymphoma																					
Adenocarcinoma																					
Soft Tissue																					
Sarcoma																					

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No.	4 - Female - High Dose (Continued)																	
Animal No.	4670	4671[d]	5147	5148	5149[d]	5151	5152	5154[d]	5155	5158	5160	5163[d]	5164	5166	5167	5169[d]	5170	5172	5173[d]	5175
Tissue Findings																				
Pituitary																				
Adenoma			+		+		+	+			+			+				+		
Thyroids																				
C-cell adenoma								+												
Thymus																				
Thymoma										+										
Liver - Preneoplastic Alterations																				
Basophilic focus				+																
Liver - Neoplasms																				
Neoplastic nodule																				
Carcinoma																				
Stomach																				
Squamous cell carcinoma																				
Integument																				
Fibroma																				
Squamous cell carcinoma																				
Uterus																				
Leiomyosarcoma																				
Adenocarcinoma																				
Carcinoma																				+

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No.	4 - Female - High Dose (Continued)
Animal No.	4670 4671[d] 5147 5148 5149[d] 5151 5152 5154[d] 5155 5158 5160 5163[d] 5164 5166 5167 5169[d] 5170 5172 5173[d] 5175
Tissue Findings	
Mammary Gland	
Adenoma	
Fibroadenoma	• • • •
Adenocarcinoma	
No Organ Specified	
Sarcoma	
Myelosarcoma	•
Malignant Lymphoma	
Adenocarcinoma	
Soft Tissue	
Sarcoma	

[illegible]-YEAR TOXICITY STUDY IN RATS

LRI PROJECT [illegible]

NEOPLASMS

Group No.	4 - Female - High Dose (Continued)
Animal No.	S176 S178 S179 S181 S182 S183 S185 S189 S190 S191 S192 S193 S194 S195 S196 S197 S198 S199 S200 S201
Tissue Findings	
Pituitary	
Adenoma	• • • • • • • •
Thyroids	
C-cell adenoma	•
Thymus	
Thymoma	
Liver - Preneoplastic Alterations	
Basophilic focus	•
Liver - Neoplasms	
Neoplastic nodule	
Carcinoma	•
Stomach	
Squamous cell carcinoma	•
Integument	
Fibroma	
Squamous cell carcinoma	
Uterus	
Leiomyosarcoma	
Adenocarcinoma	•
Carcinoma	

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No.	4 - Female - High Dose (Continued)																		
Animal No.	5176	5178[d]	5179	5181	5182	5183[d]	5185	5189	5190[d]	5191	5192[d]	5193[d]	5194	5195	5196	5197	5198[d]	5199	5200	5201[d]
Tissue Findings																				
Mammary Gland																				
Adenoma						+							+							
Fibroadenoma					+	+	+		+							+		+		
Adenocarcinoma																				
No Organ Specified																				
Sarcoma																				
Myelosarcoma																				
Malignant lymphoma																				
Adenocarcinoma		+																		
Soft Tissue																				
Sarcoma							+													

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No.	4 - Female - High Dose (Continued)																	
Animal No.	5202	5203[d]	5204[d]	5205	5206	5207	5208	5209	5210[d]	5211	5212[d]	5213	5214	5215	5217	5218[d]	5219	5220	5221
Tissue Findings																			
Pituitary																			
Adenoma	+			+		+	+			+					+		+	+	
Thyroids																			
C-cell adenoma					+							+							
Thymus																			
Thymoma																			
Liver - Preneoplastic Alterations																			
Basophilic focus	+																		
Liver - Neoplasms																			
Neoplastic nodule														+					
Carcinoma																			
Stomach																			
Squamous cell carcinoma																			
Integument																			
Fibroma																			+
Squamous cell carcinoma																			
Uterus																			
Leiomyosarcoma																			
Adenocarcinoma																			
Carcinoma																			

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No.	4 - Female - High Dose (Continued)																	
Animal No.	5202	5203[d]	5204[d]	5205	5206	5207	5208	5209	5210[d]	5211	5212[d]	5213	5214	5215	5217	5218[d]	5220	5221
Tissue Findings																		
Mammary Gland																		
Adenoma																		
Fibroadenoma	+	+	+				+				+	+			+		+	+
Adenocarcinoma				+	+					+							+	
No Organ Specified																		
Sarcoma																		
Myelosarcoma																		
Malignant lymphoma														+				
Adenocarcinoma		+																
Soft Tissue																		
Sarcoma																		